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ACUTE POSTOPERATIVE DUODENAL FISTULA

A Report of 12 Cases

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DUODENAL fistula is a most distressing but fortunately a rare postoperative complication. Colp,[12] writing in 1923, reported 61 cases, of which 53 were collected from the literature. The mortality in this series was 51 per cent. Bohrer and Milici[5] added 44 cases from 1923 to 1931. The mortality in this group was 18 per cent, giving a combined mortality of 37 per cent in 105 cases.

In what we believe to be a complete review of the literature from 1865 to 1937, a total of 130 reported cases of postoperative duodenal fistula were found. Establishing an arbitrary period of three months as the maximum postoperative interval during which a duodenal fistula may be considered of the acute type, and excluding those cases in which insufficient data are available, we reduce this total to 116 cases. To this we now add 12 cases from the records of the Massachusetts General Hospital for the past twenty years. A brief summary of each of our own cases appears at the end of this paper. Each has been carefully studied in the hope of obtaining information which may help in treating similar patients in the future. Critical remarks are added to most of the case summaries. It should be kept clearly in mind that many of these patients were treated some years ago, and statements made from the vantage point of our present more complete knowledge of this condition should not be construed as criticism of the actual treatment.

There are two general types of duodenal fistula: the lateral type, in which the opening is in the duodenal wall but the continuity of the gastrointestinal tract remains intact, and the end type, in which the fistula results from leakage from the closed duodenal stump following gastric resection or pyloric occlusion. In the latter group, the continuity of the gastrointestinal tract has of course been interrupted and re-established by some form of gastrojejunostomy.

That the end type is much less common and a much more benign condition than the lateral type is shown by the fact that the former occurred in only 14 cases in the entire series of 128 with but 2 deaths, a mortality of 14 per cent, while the mortality of the 114 cases with the lateral type was 40 per cent.

The surgical procedures which preceded the development of the fistula have been divided into groups and listed in order of numerical importance in Table 1. These procedures cannot in themselves be considered true etiologic factors. There were involved in each operation, however, certain fundamental factors which led to the production of duodenal fistulas. They may be divided into three groups, any combination of which may be present in a given case:

Table 1. *Surgical Procedures Preceding Onset of Fistula.*

PROCEDURE	NO. OF CASES
Gastric surgery including resection for cancer or ulcer, gastroenterostomy and pyloric occlusion	23
Right nephrectomy for cancer, hydronephrosis and pyonephrosis, nephrolithiasis and perinephric abscess	22
Duodenorrhaphy for perforated duodenal ulcer, with or without gastroenterostomy	17
Cholecystectomy for acute or chronic cholecystitis and cholelithiasis	15
Combined surgery on the extrahepatic biliary system and the upper gastrointestinal tract	15
Cholecystostomy for acute cholecystitis	8
Exploration of the common duct, with or without cholecystectomy	8
Incision and drainage of an abscess in the right upper quadrant	7
Suture of a traumatic rupture of the duodenum	5
Miscellaneous operations with accidental perforation of the duodenum	5
Resection of a duodenal diverticulum	1
Incision and drainage of an appendix abscess	1
Appendectomy with drainage	1
	128

(1) *Trauma.* An unrecognized perforation of the duodenum may be made at the time of operation, or the duodenal wall may be sufficiently traumatized and devitalized so that a spontaneous

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perforation occurs during the postoperative period. Drainage material placed in contact with the duodenal wall may be a contributing traumatic factor in the production of necrosis.

(2) *Sepsis.* Infection at the site of operation may cause necrosis of the duodenum and subsequently the development of a fistulous tract.

(3) *Improper healing.* That a sutured wound of the duodenal wall does not heal may be caused by the local condition or by various factors in the patient's general condition. Both sepsis and trauma may be local factors interfering with healing. That purulent infection rapidly destroys the tensile strength of catgut has been shown by Howes,[29] and that trauma and devitalization interfere with healing is too well known to require discussion. Other important local factors are faulty suture technic or material, the presence of drainage material adjacent to a suture line, and improper hemostasis with the collection of blood or serum, with or without subsequent infection. In addition, various systemic factors may affect the healing of a sutured wound in the duodenum. Howes, Briggs, Shea and Harvey[28] have shown that starvation has a retarding effect on wound healing. Lanman and Ingalls[39] have recently demonstrated the importance of vitamin-C deficiency in improper wound healing. Dehydration has long been recognized as influencing regeneration of tissue.

With the increasing knowledge of the underlying chemical changes involved in extensive loss of duodenal contents, and with improvement in methods of combating these changes, the mortality statistics have shown a gratifying decline. Table 2

Table 2. *Mortality Rates in Cases with Acute Postoperative Duodenal Fistula.*

YEARS	NO. OF CASES	MORTALITY %
1901-1905	13	46
1906-1910	5	80
1911-1915	22	59
1916-1920	17	24
1921-1925	30	37
1926-1930	26	23
1931-1935	10	10
1935-1937	5	60
Total	128	38

shows the mortality by five-year intervals since 1900, and the number of cases in each five-year period. Credit for the clinical progress reflected in these generally lower mortality figures must be given to a large number of workers. The more important findings follow.

Elman and McCaughan[15] demonstrated the fatal effect on dogs of the total loss of pancreatic juice. Loss of electrolytes and dehydration are factors leading to this result, and life can be prolonged by parenteral administration of Ringer's solution. Death cannot be prevented by this treatment, however, and occurs after some weeks. It is apparently not due to inanition and the possibility of the loss in the pancreatic secretion of some essential substance other than water and electrolytes has been suggested.

Prolonged loss of gastric secretion will eventuate in death owing to depletion of chlorides, dehydration and alkalosis, and changes in kidney function — the so-called "dehydration kidney." The gastric secretion itself is not essential to life, but chlorides and water are. This has been amply proved by White and Fender[81] and by Gamble and Ross.[21]

In experimental animals prolonged loss of bile is compatible with life, as shown by Walters and Bollman.[75] It does lead, however, to an increase in fibrinogen content and viscosity of the blood, a bleeding tendency, faulty fat metabolism and a lowered blood calcium and phosphorus.

If a sufficiently large proportion of the duodenal contents is lost through the fistula, the patient will soon suffer from nitrogen starvation due to deficient protein intake. This is reflected in a lowering of the serum protein. The work of Jones, Eaton and White[31] has shown experimentally that this is an important factor in making fluid accumulate in the tissues and producing edema. They emphasize that there are various other important elements in the production of postoperative edema, such as serous drainage, sepsis and the administration of excessive amounts of water and sodium chloride.

Thus in a patient with a duodenal fistula the following chemical mechanisms are brought into play as a result of loss of duodenal contents and starvation:

Blood chlorides fall, owing to the loss of chlorides present in the secretions of the stomach, liver and pancreas. The tissue chlorides follow a course parallel to that of the plasma chlorides.

Sodium bicarbonate is lost in the bile and pancreatic secretion. This loss, together with that of chlorides, tends to decrease the salt concentration of the plasma.

The *carbon-dioxide combining power* of the blood is increased. Loss of hydrochloric acid leaves an excess of base in the plasma which is combined with carbon dioxide to form bicarbonate. The increase in carbon-dioxide combining power does not necessarily parallel the loss of chloride, owing to the increase in ketone bodies and organic acids resulting from faulty metabolism and tissue breakdown.

Dehydration occurs, being due to fluid loss and the inability of the body to retain water in the face

of a falling salt concentration. This leads to a decreased fluid content, increased viscosity of the blood and slowing of the circulation. Cyanosis may occur, and polycythemia and a temporary elevation of the plasma protein may be present.

The *nonprotein nitrogen* of the blood rises after some days. Several factors contribute to this. Kidney excretion may be impaired by faulty circulation, and increased formation of waste products, due to tissue breakdown, may occur.

The *serum protein* falls gradually, on account of insufficient protein intake. The importance of this factor in the production of nutritional edema has been discussed above.

The rapidity with which these changes occur is the result of a balance between the proportion of duodenal contents lost through the fistula on the one hand, and the success of the efforts made to offset this loss on the other.

That extremely large amounts of drainage may occur from a duodenal fistula is well known. Erdman[16] reports the collection of 4000 cc. in a single day. Various factors contribute in determining the amount of drainage. The amount taken by mouth is the most obvious one and needs no discussion. The size and location of the fistulous opening are obvious factors.

In addition to these purely mechanical influences, the muscular activity of the duodenum plays a most important part, as pointed out by Perl.[58] He also emphasizes the increase in peristaltic activity due to duodenal irritation. Normally the duodenal contents are passed to and fro a few times, to promote rapid mixing of food and digestive juices, before passing into the jejunum. The normal intraduodenal pressure is 15 cm. of water, and rises higher during peristaltic activity. This undoubtedly explains why such a large amount of drainage may come from a relatively tiny fistulous opening in the duodenum.

The diagnosis of postoperative duodenal fistula usually presents no great difficulty. Typically the onset is sudden, coming usually within the first two weeks after operation, often immediately following the removal of a drain. It is characterized by a copious alkaline watery discharge from the wound, with rapid and widespread irritation and necrosis of the tissues of the abdominal wall. The diagnosis can usually be easily confirmed by the administration of a dye, such as carmine or methylene blue, by mouth. In the lateral type of fistula the dye appears on the dressing almost at once, while in the end type the interval may be somewhat longer, but the dye generally appears in sufficient quantity to clinch the diagnosis.

The treatment of duodenal fistula falls naturally into two phases: first, adequate local care of the wound to minimize irritation and digestion of tissue; secondly, systemic treatment to offset so far as possible the effects of the loss of duodenal contents.

It appears from our study that the most important single factor in the local care of the wound is the use of constant suction, to keep it as dry as possible and prevent prolonged contact between the duodenal contents and the tissues of the abdominal wall. Cheever[10] gives credit to Jones and Williams for first advocating this procedure, and most recent writers advocate its use.

In addition to the mechanical removal of irritating substances from the wound, a variety of local applications have been advocated. These may be divided according to their intended action as follows:

(1) Chemical neutralization of the proteolytic ferments by combining them with an excess of peptone powder, protein and fat, beef juice or Bovinine (Potter,[60] Warshaw,[78] Kittelson[34]). McEvers[47] has suggested that the same effect may be obtained by the oral administration of boiled milk, acidophilus milk or reliquefied milk concentrate.

(2) Mechanical adsorption of the ferments by finely divided charcoal, kaolin or bronzing powder.

(3) Inactivation of the tryptic ferments by producing an acid medium. Irrigation of the wound with N/10 hydrochloric acid (Potter[60]), citric acid (Johanson[30]) or 5 per cent tannic acid (Perl[58]) has been suggested.

(4) Protection of the surrounding skin by boric ointment, zinc oxide or liquid latex. In our hands it has proved difficult to apply these in such a way that the duodenal contents will not seep under them, thus making the situation worse.

(5) Elimination of positive intraduodenal pressure by passing a tube into the duodenum, as advocated by Perl.[58]

After reading the uniformly successful reports on various combinations of these methods, one must conclude that the extreme care with which the technic is applied is more important than the actual substances used, and that any logical plan of local treatment will, if carried out with sufficient patience and care, yield a satisfactory result.

The importance of early recognition of the fundamental chemical changes resulting from loss of duodenal contents cannot be too strongly stressed. The rapidity with which these changes may develop is illustrated in the abstract of Case 3. This woman was moribund ten days after the establishment of the duodenal fistula. The speed with which such a desperate situation may develop depends on the patient's general condition at the time of operation, and upon the proportion of the

duodenal contents lost through the fistula. Various chemical determinations should be used at frequent intervals to help keep the surgeon informed as to the patient's condition, and to determine the vigor with which the various chemical changes must be combated.

The best clinical guide to an adequate fluid balance is the urinary output. To keep this up to 1500 cc. in twenty-four hours in a patient who is losing a considerable amount of fluid through a duodenal fistula requires the administration of large amounts of parenteral fluid. The danger of giving excessive amounts of fluid and sodium chloride, with the resultant production of edema, has already been mentioned, and must be kept constantly in mind.

Glucose must be given in the parenteral fluid to supply tissue demands and replenish glycogen stores in muscle and liver. The carbon-dioxide combining power of the blood must be checked at frequent intervals. The blood nonprotein nitrogen gives an index of the degree of success of the kidneys in eliminating waste products.

The serum-protein level must be frequently determined. Providing an adequate parenteral supply of fluid and salt is a relatively simple problem compared with that supplying a parenteral protein. Blood transfusion is one means of giving the body protein, but in practice it has proved rather ineffective in the face of prolonged nitrogen starvation. Nevertheless, the value of a well-timed blood transfusion as a general stimulant and as a means of combating secondary anemia cannot be overemphasized.

It must be remembered that the treatment of a patient with a duodenal fistula is a long-drawn-out process. The average duration of drainage in our cases was twenty-two days, and the longest single period was six weeks. In dealing with a small fistula with relatively little loss of duodenal contents, local care of the wound, parenteral fluid, salt and glucose, together with transfusion as indicated, may be adequate therapeutic measures.

If the fistula is large and the drainage profuse, the patient's course may be steadily downward in spite of all these efforts. It is in these cases that death occurs, and often the outcome is fatal because the situation becomes desperate before it is recognized as such, and too late for adequate defense measures. Once serious disturbances in body chemistry have developed, effective relief is difficult, and these changes must be foreseen and opposed effectively before they reach grave proportions. It is our belief that in treating serious cases success depends upon early recognition of the inadequacy of the parenteral route by itself, and upon the establishment of an adequate means of introducing substances into the gastrointestinal tract below the fistula. The advantages are obvious: the drainage from the fistula can be collected and replaced in the intestinal tract, and an adequate caloric intake, including a sufficient supply of protein and vitamins, can be provided.

The exact method of effecting this result must be chosen to fit the particular case. It may be possible to pass a small nasal tube through the stomach and into the duodenum far enough to be effective; or a tube may be successfully introduced through the fistulous tract into the duodenum. The latter procedure seems somewhat hazardous, as it may well delay closure of the fistula. If a functioning gastrojejunostomy is present, the problem may be simplified and tube feeding of the collected drainage may be tried.

If these simpler methods are not effective, a jejunostomy must be done. This should be carried out through a short muscle-splitting incision in the left upper quadrant under local block anesthesia. The tube should enter the bowel at least 15 cm. below the ligament of Treitz. The exact method for its insertion by a modified Witzel technic has been well described by Linton.[43]

The dangers of delay in performing a jejunostomy are illustrated in the abstracts of Cases 1, 3, 4 and 5. It is of course impossible to say that if the operation had been carried out at an earlier date the patients would have survived, but it seems obvious that their chances would have been improved, and we believe that in many cases of duodenal fistula a well-timed jejunostomy will prove to be a lifesaving procedure.

SUMMARY AND CONCLUSIONS

1. Twelve cases of acute postoperative duodenal fistula treated at the Massachusetts General Hospital, together with 116 cases from the literature, are reviewed.

2. There are two general types of duodenal fistula: the lateral and the end types. The latter is less common and more benign.

3. Various local and systemic factors of importance in the production of a duodenal fistula are discussed.

4. Treatment is divided into two phases: local and systemic. Constant suction is the most important single factor in local treatment.

5. The changes in body chemistry resulting from the loss of duodenal contents are briefly discussed.

6. The importance of the prevention of these changes by actively combating them in the early stages is stressed.

7. The early recognition of the need of a jejunostomy is emphasized. We believe this to be a lifesaving procedure in many cases.

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CASE REPORTS

Case 1. A man of 35 had had a cholecystectomy and choledochostomy performed in 1918. A catheter was sewed into the common duct. Cholecystostomy had been done 3 years previously at an outside hospital. Thirteen days after the operation, following removal of the catheter and the cigarette wick, profuse bile-stained drainage from the wound began. That this was a duodenal fistula was immediately recognized.

The patient's course was steadily downhill in spite of parenteral fluid containing glucose and salt, and attempts at rectal feeding. One month after the appearance of the duodenal fistula, jejunostomy was done under ether anesthesia. Twelve days later the patient died.

Comment. The loss of duodenal contents, including in all probability a large part of any food taken by mouth, was allowed to continue for a month, without attempting to collect this material and replace it in the gastrointestinal tract. This case occurred a number of years ago, and no blood-chemistry determinations are available. In view of the length of time that the patient lived after the development of the fistula, it seems more than likely that if a jejunostomy had been done as soon as the fistula appeared, and if the duodenal drainage had been collected and replaced in the jejunum, together with an adequate supply of nourishment, he might well have survived.

Case 2. A man of 40 underwent a cholecystostomy and drainage of subhepatic abscess in 1922. No stones were found. The gall bladder was acutely inflamed. He had a long and stormy convalescence with a persistent biliary sinus and was discharged 3 months after operation, with instructions to return in 1 week for cholecystectomy. On readmission the sinus tract was explored in an attempt to remove the gall bladder. The operation was abandoned on account of uncontrollable oozing. A portion of the sinus tract was removed, and on pathological examination showed tuberculosis. Nine days later a duodenal fistula developed.

Fourteen days after operation an attempt was made to do a jejunostomy through an incision in the left upper quadrant. Dense adhesions were encountered, and the operation was stopped because of profuse bleeding, without an available loop of bowel having been found. Attempts to get a nasal tube into the duodenum were unsuccessful. Constant suction was used to prevent digestion of the abdominal wall, but repeated hemorrhages from the fistulous tract occurred. Many hypodermoclyses and several transfusions were given, but the patient's condition became steadily worse and he died 3 weeks after the appearance of the fistula.

Autopsy showed extensive tuberculous peritonitis, duodenal fistula and a subhepatic abscess cavity.

Comment. It seems according to present concepts that every attempt was made to treat this patient properly. These efforts were unsuccessful because of the nature of the underlying process, which was not definitely identified until autopsy.

Case 3. A woman of 28 had a nephrectomy for tuberculosis of the kidney in 1922. The procedure was technically difficult as the surgeon's note states that the "kidney was freed by cutting masses of scar tissue." Immediate and profuse bile-stained drainage from the wound was noted. In spite of a high fluid intake by mouth the urinary output was low. Carmine given by mouth appeared on the dressing in 10 minutes. A diagnosis of duodenal fistula was made. The patient's condition became rapidly and progressively worse. Ten days after the operation jejunostomy was considered, but the patient was deemed too sick to stand the procedure, and she died the next day.

Comment. This case illustrates how rapidly a patient's condition can become critical when the defect in the duodenum is large and the drainage profuse. It also illustrates the danger of even a few days' delay in performing a jejunostomy in a case of this type.

Case 4. Six months before entry a man of 55 had had a cholecystostomy for acute cholecystitis, which was followed by a persistent biliary fistula and intermittent jaundice. At operation, performed in 1924, a dilated common duct with an obstruction at its lower end was found. No opening into the duodenum could be discovered and a choledochoduodenostomy was done. The gall bladder was drained.

The wound drained profusely with much skin irritation, and a diagnosis of duodenal fistula was made. The drainage amounted to about 4000 cc. daily, and constant suction was used to keep the wound dry. Parenteral fluid containing salt and glucose was given and transfusion was done. The patient's condition became rapidly worse and he died 19 days after operation.

Autopsy showed obstruction of the common duct due to adenocarcinoma.

Comment. In retrospect and in the light of our present knowledge, a jejunostomy should have been done as soon as the profuse drainage was recognized as duodenal contents.

Case 5. Cholecystectomy and choledochostomy were done in 1928 on a man of 49. The operation was technically difficult, and an opening was made in the duodenum in freeing it from the gall bladder. There was some question as to whether a spontaneous fistula between the duodenum and gall bladder had been present. Stones were removed from the common duct and a catheter was inserted for drainage. The duodenum was closed in two layers and the suture line was carefully covered with omentum.

Ten days after operation an abscess developed in the wound, followed by profuse drainage. A diagnosis of duodenal fistula was made, and 10 days later the wound was put on suction. Three weeks after the development of the fistula a jejunostomy was done. Two days after this, fecal drainage from the original wound began, and 3 days later the patient died.

No blood chemistry was done until the day the jejunostomy was performed. At that time the blood nonprotein nitrogen was 90 mg. per cent, and the blood chlorides were 462 mg. (as sodium chloride) per cent. Three days later the nonprotein nitrogen was 188 mg., and the blood chlorides 578 mg. per cent. This patient was given clyses for 10 days after the first operation, and no more parenteral fluid until the day of the second operation.

Comment. Here again it seems fair to say that if the seriousness of the situation had been recog-

nized sooner and a jejunostomy had been done at once, rather than allowing the loss of duodenal contents to continue for three weeks, the patient's chances of survival would have been improved. At the present time a loss of duodenal contents would certainly not be allowed to continue so long without administration of parenteral saline and glucose.

Case 6. A woman of 33 developed a duodenal fistula following a third operation on the biliary system. The first operation was a cholecystectomy done at another hospital. The second was an exploration for biliary obstruction. A dilated stump of hepatic duct was found, but it was impossible to anastomose this to the duodenum, so a tube was inserted and a biliary fistula established. At the third operation in 1929 this fistulous tract was implanted into the duodenum. Profuse bile-stained drainage began at once, and carmine given by mouth appeared on the dressing immediately.

A diagnosis of duodenal fistula was made, and a week later jejunostomy was done and the original wound was put on suction. The collected drainage was introduced into the jejunostomy tube, together with a concentrated liquid-food mixture. Five weeks after operation drainage from the incision stopped, and 3 days later the jejunostomy tube was removed.

The blood chlorides were repeatedly measured, and were kept within normal limits by parenteral fluids as indicated. Ten days later the fistula opened spontaneously and drained for 3 days before closing.

The patient was discharged from the hospital 6½ weeks after operation. Her progress after leaving the hospital was complicated by intermittent bouts of biliary obstruction, and she finally died 3½ years after operation.

Case 7. A man of 27 had an exclusion of the pylorus and a posteriorgastroenterostomy performed for duodenal ulcer in 1929. After 7 days of uneventful convalescence he began to run an unexplained temperature, and soon developed some fluid in the left pleural cavity. Three weeks after operation the wound broke open and began to drain profusely. Carmine by mouth appeared on the dressing within 1 hour. A diagnosis of duodenal fistula was made.

Constant suction was instituted and the wound progressed well. No blood-chemistry determinations are recorded. Drainage ceased, and 7 weeks after operation and 4 weeks after establishment of the fistula the patient was discharged with the wound nearly healed.

Comment. This is the only case in our series of the end type of duodenal fistula, and illustrates the relatively benign course of most of these cases.

Case 8. A man of 77 had a resection of the pyloric end of the stomach and a posterior gastroenterostomy performed in 1934. On the 11th postoperative day the wound separated, requiring resuture. Profuse drainage from the wound continued and a diagnosis of duodenal fistula was made.

The case was treated by intravenous glucose in normal saline and by transfusion. Two weeks later the blood chlorides were equivalent to 107 cc. of N/10 hydrochloric acid, and the serum protein was 5.2 gm. per cent. A tube was successfully passed through the fistula into the duodenum and feedings were started. Immediate improvement was noted. The serum protein remained at 5.1 gm. per cent. The duodenal tube was removed 4 weeks after the establishment of the fistula. There was no further drainage. The patient was discharged 73 days after operation.

Comment. This case illustrates the success with which the situation can be kept under control if a tube can be passed through the fistula into the duodenum.

Case 9. A woman of 52 was operated upon for carcinoma of the stomach in 1936. A posterior gastroenterostomy for duodenal ulcer had been done 25 years previously. Abdominal exploration revealed a carcinoma of the stomach, which was amenable to surgical removal. The posterior gastroenterostomy appeared normal. The duodenum was shrunken to a small, thickened, finger-like process. The gastrocolic and gastrohepatic omentums were divided, but at this point the patient's condition became so poor that it was deemed wise to abandon further operation. The wound was closed and the patient was returned to the ward. On the 15th day after operation wound sepsis developed, and the next day profuse bile-stained drainage from the wound began. A diagnosis of duodenal fistula was made.

For the next 2 weeks the blood chlorides and the carbon-dioxide combining power were kept within normal limits by means of parenteral fluids. The blood nonprotein nitrogen was not elevated, and the urine was negative. The serum protein fell to 4.1 gm. per cent. The patient went steadily downhill, and died at the end of this 2 weeks' period in spite of repeated transfusions.

Comment. It is hard to see how the treatment of this patient, once the duodenal fistula was established, could have been improved, at least as indicated by the various chemical factors measured. With a functioning posterior gastroenterostomy a jejunostomy would probably have been of no advantage. Collection of the duodenal contents discharged from the fistula and refeeding by means of a nasal tube in the stomach, however, might have improved the patient's chances of survival, and should have been tried.

Case 10. A woman of 72 was admitted in 1936 with a diagnosis of acute cholecystitis. She was jaundiced, with a van den Bergh of 8.92 mg. per cent and an icteric index of 20. The blood nonprotein nitrogen was 26 mg. per cent. The acute attack subsided, and 10 days after admission operation was undertaken. It proved to be a difficult procedure. A much dilated common duct was found and opened. No stones were found in it. The ampulla of Vater was easily dilated and the duct was closed around a T tube. There was a stormy convalescence, with pulmonary collapse at the right base and a low urinary output, in spite of the administration of intravenous glucose in normal saline. The blood nonprotein nitrogen rose to 90 mg. per cent and the blood chlorides fell to the equivalent of 69 cc. of N/10 hydrochloric acid.

The wick was removed on the 8th postoperative day and some bleeding from the sinus tract occurred. Two days later some digestion of the skin around the sinus was noted. Twenty-two days after the operation, profuse bile-stained drainage began from the sinus with digestion of the wound. Two days later the patient died.

Comment. In this case it appears that the duodenal fistula was only the terminal event. Even

previous to its development the patient's condition was so impaired that her chances of survival were poor, and it is hard to believe that any known treatment of the fistula itself could have altered the outcome.

Case 11. A man of 57 was admitted in 1937 because of jaundice. Five years previously a cholecystostomy had been performed. Two months before admission a cholecystectomy was done because of persistent symptoms. Exploration of the common duct was thought desirable at that time but was not attempted because of the technical difficulties encountered.

At operation the region of the common duct was carefully explored. No patent common duct could be found, even by the transduodenal route, and no dilated bile ducts were located. The subhepatic space was drained. On the 7th day after operation there was a sharp increase in the amount of drainage. That this was caused by a duodenal fistula was quickly recognized, and wound suction was started.

Drainage from the fistula exceeded the oral intake by about 700 cc. in 24 hours. Adequate parenteral fluid was given and the blood-chloride level was kept within normal limits. Four days after the onset the serum protein had fallen to 4.6 gm. per cent. A transfusion of 550 cc. of blood was given. Ten days after establishment of the fistula a definite decrease in the amount of drainage was noted, and the next day the oral intake exceeded the amount of drainage. This positive balance continued to increase rapidly, and the patient's general condition improved steadily. All drainage ceased 19 days after the onset of the fistula and the patient was discharged the next day.

Comment. This case illustrates how adequate parenteral fluids and local care will control the situation, at least for a relatively short period of time, in the face of a moderately severe duodenal fistula.

Case 12. A woman of 56 had had a cholecystostomy performed 2 months before operation in 1937. At that time choledochostomy and transduodenal removal of a common duct stone were performed. Nine days after operation, following removal of the wick and tube from the common duct, profuse drainage from the wound began and a diagnosis of duodenal fistula was made.

The drainage amounted to about 500 cc. in 24 hours and was collected by constant suction. The blood chemistry was easily maintained at normal levels by parenteral fluids. Nine days after establishment of the fistula all drainage had ceased, and 5 days later the patient was discharged from the hospital.

Comment. This case is an excellent example of a fistula with only a relatively small amount of drainage, in which the situation was easily controlled by local measures and parenteral fluid.

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THROMBOPHLEBITIS IN THE LEGS

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As you are well aware, for both the surgeon and the physician thrombophlebitis presents a serious clinical problem. I need not dwell on this. I should like rather to remind you of the basic nature of thrombosis, without knowledge of which a discussion of its clinical behavior is meaningless.

First, and most important, thrombosis takes place only in a blood current—a slow one as a rule. It is not coagulation, or clotting, in which the formation of fibrin is the principal reaction, but rather a deposition of blood platelets, that is, thrombocytes, on the wall of a vein. These thrombocytes, having become plastered together and fixed, build out into the stream a spongelike structure to which the white corpuscles adhere and in whose narrow interstices clotting *then* occurs. The process soon occludes the vein. The oldest portion, or head, of Zahn's classic thrombus is white and tough, since it consists mostly of platelets, and the neck, or mixed portion, which contains an increasing amount of fibrin and red cells, is dark red and still solid; but the tail, which is without platelet lamellae and which may extend for a long distance away from the neck, is necessarily clotlike and unsubstantial. Should it grow into a current, it may become so soft and flimsy that finally it can hardly be distinguished from normal blood. Insofar as this friable portion builds itself away from the heart it merely blocks more and more of the peripheral venous tree, but if it grows toward the heart, unfixed in the vein and waving in the current of an entering branch, fragile and ready to break from the body, it is a potential embolus—a serious threat to life. The tendency of most thromboses in their heartward progress is to stop abruptly and heal when they meet a vigorous current, but to grow out into a feeble one as the *propagating thrombus* just described, ready to become a source of minor infarction or of fatal pulmonary embolism.

From the Surgical Clinic of the Peter Bent Brigham Hospital, Boston.

Read before the Boston Surgical Society, December 6, 1937, in connection with a demonstration by Dr. C. H. Best, of Toronto, of the use of heparin in preventing experimental thrombosis in animals, in preventing thrombosis in glass tubes, and in controlling postoperative thrombophlebitis in human beings. An account of this work by Dr. Best and his associates has already been published. (Best, C. H.; Cowan, C., and MacLean, D. L.: Heparin and formation of white thrombi. Science 85:338-339, 1937.)

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CAUSES OF THROMBOSIS

There is in the literature much tiresome discussion of the influences which lead to thrombosis in veins. I am reminded of the first medical paper to which I ever listened, in which the author, a medical student, showed that practically every abnormality or disease of the human body was a source of constipation. Nevertheless, among the countless reported causes of thrombosis there are

a number of fairly recognizable influences that may be held responsible.

Disorders of the Vein Wall. In the case of severe local injury, sepsis or actual varicosity, such a basic disorder is clear enough. Thrombophlebitis of the sigmoid sinus in middle-ear disease and the phlebitis of varicose veins are familiar examples. But most thromboses occur in the absence of any such known influences. Aside from rheumatic changes in the vein wall, changes which I have known to be a cause of a very deceptive thrombosis and a fatal embolism, evidence of the significance of degenerative changes even in acute fevers is rather speculative. However, in phlegmasia alba dolens, perhaps the commonest of all thrombophlebitides, I have found, on several occasions, when exploring the pelvis, a remarkably acute nonsuppurative inflammation surrounding the external iliac artery and vein and extending down the great femoral vessels into the thigh. This change has given me the impression of being the cause not only of the venous thrombosis but of arterial spasm as well. I cannot account for this phenomenon, which Cruveilhier noticed many years ago, though it is tempting to lay it to a lymphangitis reaching the iliac lymphatics from the legs or pelvis; and since there is little evidence to show how often it is present, it had perhaps best be kept in mind for future investigation and not taken too seriously at the moment.

Possibly in considering the disorders of the vein wall the factor of age ought to be included. For though thrombophlebitis does occur in young adult life, especially as a complication of childbirth and abdominal operations, middle to advanced age — the years from forty-five to sixty-five — is most liable to it.

Disorders of the Blood. Perhaps the most concrete disorder of the sort described is dehydration, such as may result from vomiting, diarrhea, hemorrhage, deprivation of fluids or sweating at the operating table. There is also the rather vague but obviously important influence of injury, in the form of crushes, fractures and, of course, surgical operations. The influence of trauma may be local, as when thrombosis occurs in the great veins of the calf or thigh on the side of a fracture, or general, as when a femoroiliac thrombosis follows an abdominal or thoracic operation or an injury. Again, its influence may be immediate, or perhaps remote and related to the atrophy of disuse.

Conceivably, thrombophilic changes in the blood are related to clotting rather than to thrombosis. Bancroft and his co-workers have established a "clotting index," particularly in some preoperative and postoperative states. They believe that by the use of certain dietary and medicinal steps they not only can lower a high index but can actually diminish the incidence of thrombosis. However that may be, abnormal states of the blood are more easily corrected than are other supposed thrombophilic influences, and, whether chronic or acute, should be kept in mind.

Disorders of the Venous Return. These are of the greatest interest. They may be due to general circulatory failure, to cardiac weakness plus venous stasis or to venous stasis alone. Since thrombosis is most apt to occur in a *slowed* current, they are obviously fundamental. A patient sitting up or reclining in bed subjects the return flow from the relaxed legs to a decided slowing. Increased abdominal tension, as in any state of gaseous distention, during pregnancy or parturition, or following abdominal operations, obviously aggravates this unfavorable influence. But the anatomic relations of the upper femoral and iliac veins are perhaps even more important. There are many entering vessels, as is shown in the sketch. These branches, together with the few large valves of the region, are believed to cause eddies which encourage the deposition of platelets. The hypogastric arteries cross the external iliac veins, and the right common iliac artery crosses the left common iliac vein. These relations impede the natural current, on the left more than on the right. There is also present, in the upper calf and popliteal space, an area somewhat like that of the groin where many currents meet, and where many obscure thromboses undoubtedly originate. Aschoff has discussed all these influences most interestingly.

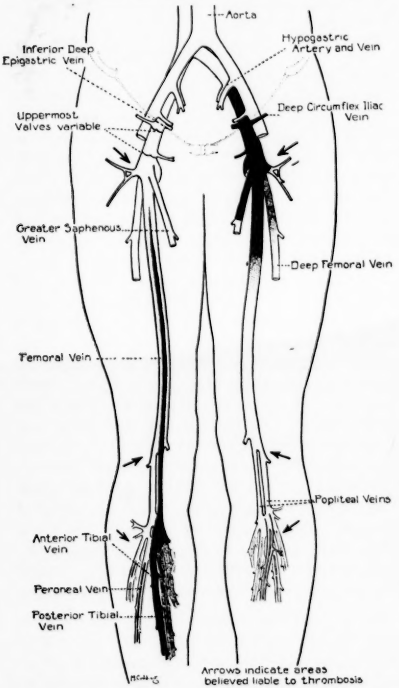
To sum up the principal factors favoring thrombosis: there are, first, inflammation of the vein wall, a factor of great potential importance, little understood as yet, and undoubtedly influenced by advancing years; secondly, changes in the blood itself, whether in the nature of depletion or related to the obscure influence of trauma; and thirdly, the slowing of the venous return from the legs, dependent upon confinement to bed and aggravated by increased abdominal tension. Such factors tend to cause thrombosis in certain especially susceptible vessels, notably the femoroiliac veins and those of the calf and popliteal space.

VARIETIES OF THROMBOPHLEBITIS

These I have fully described elsewhere, so that I shall merely comment upon their individual peculiarities.

Phlegmasia Alba Dolens, Femoroiliac Thrombophlebitis, or Milk-Leg. This very common form commences in the upper femoral and external iliac

vein. It leads to edema of the entire limb, but doubtless the severity and duration of the swelling depend on the amount of the venous tree occluded. It must be supposed that the less extensive the thrombosis, the more quickly and completely will a collateral circulation be established; and the more widespread the thrombosis, the more serious and prolonged will be the obstruction. Edema rather than blueness seems to measure the severity of the process. It is beginning to appear that a deep femoral or iliac thrombosis *may* be present without swelling, and Barker has shown that it can even establish itself — though rarely, to be sure — during active life. Moreover, it now seems probable that thrombosis begins much nearer the time of the operation, childbirth, injury or confinement to bed than was formerly supposed; that is, instead of coming on ten days or two weeks afterward, it is more nearly simultaneous with the onset of the exciting factor. Recently a patient of mine died of embolism from a femoroiliac thrombosis* on the day after an abdominoperineal operation, and there was suggestive evidence that the embolism actually occurred while he was still on the operating table. Possibly the time required for the initial thrombosis to lead to an extensive and obvious venous occlusion is longer than has heretofore seemed likely. Probably this time is decidedly variable. One can say definitely that when the entire leg is edematous, a fully developed femoroiliac thrombosis is present. But the absence of swelling does not rule out thrombosis.



The Veins of the Lower Extremities (anterior view, semidiagrammatic). The areas most liable to thrombosis are indicated by arrows. On the left, a thrombosis in two of the great plexuses of the calf has extended into the femoral vein as a long, propagating thrombus (reconstruction from an actual case of fatal pulmonary embolism). On the right, the thrombosis of phlegmasia alba dolens is represented as ending cleanly where the hypogastric artery crosses the external iliac vein; the peripheral extent of the process is intentionally left vague.

One particularly interesting feature is the variation in the position and severity of the initial pain. It is sometimes severe enough to suggest serious arterial ischemia, a state which is even more definitely indicated when the arterial pulses in the foot become feeble or disappear. Such a state supports the hypothesis of a perivascular inflammation in the etiology of the disease. And of course a moderate fever and elevation of the pulse rate are very common.

Once a thrombophlebitis is established, the patient seems to become as it were thrombophilic. The other leg is involved far oftener than is generally supposed, but perhaps with so little swelling that the second process is overlooked. Occasionally a thrombophlebitis passes back and forth, recurring in the leg first attacked. Aschoff indicates that in a bilateral process the thrombosis ascends on the left at least to the point where the hypogastric artery crosses the external iliac vein, but on the right only to the inguinal ligament.

As to treatment, it is enough to say that elevation of the lower limbs above the level of the body for the purpose of drainage is essential, and that the affected leg should not be immobilized but exercised gently at the earliest possible moment. The thrombosis ends proximally well within the pelvis. It is very unlikely that a propagating thrombus is present. If present, it will presumably become detached whether or not the patient remains quiet. If it is not present, the proximal end of the thrombus will probably be healed by exercise and an improved circulation. Once edema has disappeared, the use of the limb, first in an elevated

*A fresh thrombophlebitis was found at autopsy in the external iliac vein. The embolus need not necessarily have come from there. Neither leg was swelled.

and then in a dependent position, may gradually be resumed. For some months a bandage or elastic stocking for the lower leg is often required.

Deep Peripheral Thrombophlebitis: Thrombosis in the Calf Muscles. This treacherous disease has been little described. Its anatomic features are illustrated on the left in the accompanying sketch. Some of the great plexuses among the muscles of the lower leg become thrombosed. A very extensive process causes swelling and perhaps cyanosis of the ankle, or even of the calf. But as a rule the disease is very silent. The exciting cause is usually some minor injury or strain of the lower leg or foot. Following this, there is a little soreness of the calf muscles on use, especially on going upstairs. The ankle swells slightly. Merely going to bed often causes all signs of the disease promptly to disappear. There is no tenderness and only perhaps a little soreness on stretching the Achilles tendon. As a rule, elevation causes the proximal end of the thrombotic process to heal, but occasionally on renewed use of the leg the whole picture reappears. This suggests extension of the thrombosis and the possibility that a propagating thrombus has formed. Indeed, it appears that embolism from such a disease is far commoner than from a femoroiliac thrombosis, yet I cannot agree with Aschoff that an embolus long and large enough to cause death can come only from the femoral region.

Repeated examinations are required in order to determine the frequency with which thrombosis occurs in the deep veins of the lower leg. My impression is that it is much commoner than is generally supposed, that it almost never merges into a femoroiliac thrombosis, and that it usually heals on proper treatment, but that it is a relatively common source of pulmonary embolism. How often the femoral vein should be divided to forestall such an accident, I have no means of knowing: probably only when elevation is not followed by the permanent relief of symptoms.* Elevation is best obtained by raising the foot of the bed 15 cm. and placing the unbandaged leg on a soft pillow. After ten days or so the leg is exercised freely in bed, and a semielastic bandage is used as life in the upright position is gradually resumed.

Superficial Thrombophlebitis in Non-Varicose Veins. This is a freakish disease, which includes phlebitis migrans. A tendency to superficial thrombosis is perhaps familial, and some individuals are subject to recurrent attacks. Like other forms, it is decidedly common in the legs. A migrating phlebitis is oftenest seen in those suffering from thromboangiitis obliterans. Injuries and perhaps exposure to cold seem to be exciting causes of the more definitely localized processes. Such as these are obstinate in resolving, and tend to spread if the patient leads an active life or remains sitting up in bed. They disappear rapidly on elevation. For those which occur at or above the knee, high division of the great saphenous vein may usefully be combined with elevation. Fatal embolism is rare, but pulmonary infarctions occasionally occur.

Thrombophlebitis in Varicose Veins. This is the least obscure and least interesting of the thromboses. The wall of the varicose vein is fibrosed and badly nourished. Very often its intima is cracked by unusual strains. Even without one's invoking the presence of infection in tissues of lowered resistance, there is sufficient reason for a considerable incidence of thrombosis in varix. That high pressures in the standing position are the usual cause of thrombosis in the slowed or reversed current is sufficiently proved by the fact that a varicose thrombosis is common in those who are active but rare in the bedridden. Once started in some pocket or distended area of a varicose vein, the thrombosis progresses until it meets a vigorous current. Thus it often reaches the femoral vein, which, however, it does not enter. Nor is embolism any but a rare occurrence. Infarctions I have seen, but not one fatal embolism.

Treatment of thrombosis in a varicose vein virtually ignores the possible detachment of an embolus. If the thrombosis is localized in the calf, an elastoplast bandage can be applied, and the patient allowed to go about his business. It is astonishing how rapidly under these conditions a cure occurs. If the process has reached the groin, elevation of the leg, as in other thromboses, is effectual. On the other hand, if high division of the saphenous vein above the thrombosed area can be accomplished, the immediate cure is more rapid and a recurrence is forestalled.

DISCUSSION

I have briefly discussed the treatment of the various sorts of thrombophlebitis in order to emphasize my conviction that thrombosis is encouraged to spread by slowing of the current of blood in and near the thrombosed vein, and is checked and healed when a vigorous venous return is created in the diseased part. In the vital matter of prevention, it would be ridiculous not to carry this conviction into action. I have noticed with interest and pleasure that one of my colleagues, with whom I have discussed the high incidence of pulmonary embolism following prostatectomy, is elevating the

*Femoral division below the profunda femoris, promptly performed, would insure against embolism in all cases. So far as the venous circulation is concerned, the operation is harmless. Shall it be carried out in ten cases to save one or two?

foot of the bed following this operation. His practice is to raise it 15 cm. for at least one half of each twenty-four hours. There is thus no bending at the groin and the feet are raised above the thorax. An extra pillow under the neck and head is of course allowed. That a similar course can be usefully followed in the pelvic surgery of women is proved by a recent publication of Schmid. In a series of 500 cases he shows that when postoperative elevation (25 cm.) of the foot of the bed was used, thrombosis and fatal embolism disappeared, as against an expected incidence of from 12 to 23 thromboses and from 2 to 7 embolisms when a similar number of patients are kept flat in bed or allowed to recline. Indeed, no *reclining* during life in bed has been allowed in the present series. Routine precautions previously devised were naturally continued.

Now, in the attempt to forestall postoperative thrombosis, measures directed against dehydration and increased abdominal tension are common-sense precautions; if preferred, Bancroft's dietary regime and sodium thiosulfate to correct a high clotting index can be used. But is it advisable to keep patients subjected to upper abdominal operations, to say nothing of those having weak hearts and failing circulation, for long periods with their feet higher than their heads? Probably not, but perhaps for short ones — say from two to six hours in every twenty-four. Even a little help for the venous return is worth while. There is a tendency nowadays to work the modern adjustable bed to extremes, and to overemphasize the advantages of the half-sitting posture. This may partly account for what seems to be an increased incidence of thrombosis in the lower limbs.

As to the period at which preventive measures are most needed, I have already suggested that thrombosis follows more closely upon the exciting factor of trauma than has been generally believed. Best and his associates, in testing the effect of purified heparin on human beings, start its administration only an hour or two after operation. A similar course is being followed by Crafoord, of Stockholm. He first gives heparin three hours postoperatively and continues its use for four days. The period covered seems to me the one during which thrombosis is most likely to begin.

The treatment of established thrombosis, in order to be consistent with the foregoing conception of its onset and progress, must hurry the return of blood from the lower limbs and pelvis. Thus it should include especially elevating* the foot of the bed and abolishing the reclining position still so often used, applying heat rather than cold (I have seen frostbites from the application of ice-bags!), and permitting a reasonable freedom of motion rather than immobilization. If this kind of treatment appears to ignore the danger of embolism, the reason is plain enough. The only sure proof that a propagating thrombus, threatening fatal embolism, is present, is the onset of pulmonary infarctions. If such occur, an attempt to divide the vein proximal to the waving, fragile thrombus is in order. But if, as is usually the case, the dangerous propagating thrombus is silent until its fatal detachment takes place, I submit that rather than attempt to prevent this detachment by immobilization — which of course is futile, since even the patient's use of the bedpan is an athletic feat — the influences most likely to prevent its *formation* should be tried, namely elevation and mobility, or at least absence of immobility. It is not the turning over in bed that causes the fatal embolism, but rather the creation of a propagating thrombus in the slowed venous current which happened many hours, or more likely many days, previously.

A few words on the relation to pulmonary embolism of thromboses about the prostate, particularly in elderly men, and about the uterus and vagina should be mentioned. Such thromboses are probably common, and have often been shown to progress into the iliac vein, where they are a cause of phlegmasia alba dolens. In this form they are very unlikely to be a source of embolism. The question is rather whether they may, from a small and perhaps undetectable beginning, become the insecure anchoring point for a propagating thrombus which occludes no large vein but which floats through the hypogastric into the common iliac vein and is detached nearly or entirely in toto. Vain searches at autopsy for the source of long pulmonary emboli (from 25 to 30 cm.) tempt one to say "Yes." Obviously more evidence is required. My own feeling has been that the popliteal region and upper calf are more likely to be the site of the long, folded thrombus such as is usually found fixed in the pulmonary artery in a fatal case of embolism. Even when autopsy reveals pronounced thrombosis in the veins of the pelvis, or perhaps the left external iliac vein, the source of embolus may still be an unnoticed process in one of the great plexuses of the calf. Such considerations suggest that more embolism occurs from undiagnosed than from evident, established thromboses.

* * *

I have taken the attitude that thrombophlebitis results from a combination of several factors, among which a slowed current, trauma and certain anatomic relations are pre-eminent. I have

*The treatment of a local varicose thrombosis by an elastic bandage and full use secures an active venous return without elevation.

ignored in the discussion of both etiology and treatment the possibility that the thrombocyte may be restrained by chemical means from throwing himself down to die in tempting locations. I am sure that since Best and his associates in Toronto have taken up the problem of forestalling thrombosis and even treating its established forms by the use of purified, nontoxic solutions of heparin, you will hear encouraging accounts of investigations along this line. Whether or not these prove fruitful, there is no harm in keeping in mind the fundamental principles relating to the etiology, progress and treatment of thrombosis.

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BENIGN STRICTURE OF THE ESOPHAGUS COMPLICATING DUODENAL ULCER

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ESOPHAGEAL stenosis is a rare complication of duodenal ulcer. Our purpose in reporting the following case is to call attention to this complication, and to emphasize the importance of treatment by esophagoscopy under local anesthesia, with bouginage by direct vision.

CASE REPORT

R. T. (U-22312), a 56-year-old, native-born clerk, first entered the Baker Memorial Hospital on February 16, 1937, complaining of epigastric pain and hematemesis. The pain was of 5 years' duration and was relieved by a bland diet and powders. The hematemesis was of a few days' duration 1 year previously, and of 5 days' duration at the present attack. Physical examination on admission showed a poorly developed, pale, emaciated man with dry skin and tongue. The blood pressure was 100/40. The red-blood-cell count was 3,410,000, the hemoglobin 60 per cent, and the white-cell count 14,800. Two stool examinations were positive for occult blood. The patient was put on hourly feedings of milk and lime water, and a 500-cc. citrate transfusion was given. On this regime the bleeding stopped and the patient improved enough for x-ray examination 1 week after admission. The x-ray report by Dr. J. R. Lingley was as follows: "The esophagus appeared normal. The stomach showed generalized prominence of its rugae. . . . The duodenum . . . was constantly deformed. Projecting from the superior anterior margin of the cap there was a large, deep, penetrating ulcer crater. . . ." Re-examination 1 week later showed the ulcer to be smaller than formerly thought, measuring only 3 mm. in diameter. On March 4 the patient was discharged home relieved on a six-meal, bland diet.

Because of a recurrence of vomiting the patient was readmitted on April 1, 1937. There had been no further hematemesis, but the red-cell count was only 2,500,000, and the hemoglobin 50 per cent. Two transfusions were given. On April 6 he was still vomiting coffee-ground material. On April 9 operation was performed by one of us (E. M. D.) and a gastric resection with posterior Polya anastomosis was done. Five days after operation there were some distress and gastric accumulation but no vomiting. A nasal tube was passed into the stomach twice a day for 4 days and then left in place for 2 days. A 500-cc. citrate transfusion was again given, and fluids were given intravenously. It was apparent that the stoma was not functioning as there was a daily increase in the gastric output. Twelve days after the gastric resection a second operation was done under local anesthesia. At operation the stoma was normal but there was a distinct kink in the distal loop of the jejunum. An enteroenterostomy was done, following which the patient made a rapid, uneventful convalescence, and was discharged home on May 8.

He was admitted for the third time on September 2, 1937. One week after arriving home, about 3½ months previously, the patient began to experience difficulty in swallowing semisolid foods, and limited his diet to eggnogs and other liquids. He began to lose weight. One month prior to entry it became impossible for him to swallow anything except water and ginger ale. His weight on this admission was 93 lb., a loss of 37 lb. since his first admission 6 months previously, and a loss of 20 lb. in the past month. Physical examination showed an exceedingly dehydrated, emaciated man, retching and vomiting saliva. Constant intravenous fluids were begun at once. X-ray examination of the esophagus (Fig. 1) was reported as follows by Dr. Lingley: "Barium met almost complete obstruction in the lower third of the esophagus, where the lumen was reduced to a very fine tube for a distance of about 5 cm. The upper margin of the defect was cone-shaped, and its lateral margins finely irregular. An ulcer crater, however, was not visualized and there was no filling defect suggestive of cancer. After 1 hour only a very small trace of barium had reached the stomach and the esophagus above the lesion was mod-

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erately dilated. The findings are those of a stricture in the lower third of the esophagus, probably due to a benign peptic ulcer." (Plates taken on the first admission had shown a normal esophagus.)

Esophagoscopy under local anesthesia was performed by one of us (E. B. B.) on September 8. About 1 cm. above the stricture there was marked reddening and inflammation of the esophagus. The opening of the stricture was almost obliterated. There was no evidence of ulcer or carcinoma. Under ocular guidance a No. 8 French silk-woven esophageal bougie was directed into the lumen and

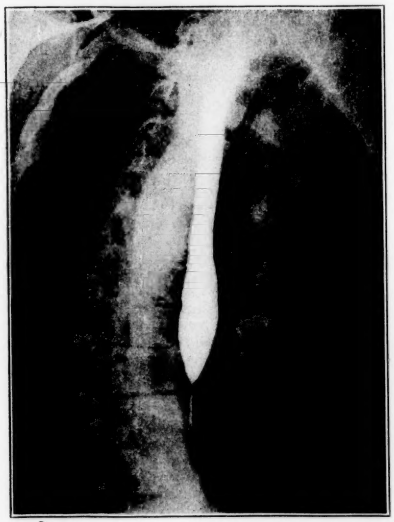

Figure 1. *X-ray of the esophagus before treatment, showing almost complete obstruction in the lower third.*

passed readily into the stomach. That the narrowing was due largely to esophagitis was soon evident, for once the lumen was established bougies up to No. 16 French passed readily. Following this the patient was able to take small amounts of liquids by mouth. Two days later, esophagoscopy was repeated under local anesthesia, bouginage was carried out as before up to a No. 16 French, and a soft duodenal tube (No. 14 French) was introduced through the stricture into the stomach. Feedings were then given through the tube. Four days later esophagoscopy was again done under local anesthesia, bouginage was carried out up to a No. 22 French, and a No. 18 French duodenal tube was placed through the stricture. Intravenous fluids were discontinued and liquids, including beef juice, fruit juices and milk, were given through the tube. In spite of a low serum protein (4.9 gm. per cent), there was never any sign of nutritional edema. Three days later a fourth esophagoscopy was done as before; the esophagitis was found to be almost entirely healed, and the stricture was dilated to a No. 24 French bougie. No feeding tube was placed and the patient began eating soft solids without difficulty. At two subsequent esophagoscopies on September 21 and September 27, a small (7-mm.) esophagoscope was passed through the stricture into the stomach.* Following the last esophagoscopy a lumen was obtained which permitted a six-meal bland diet of minced meat and strained vegetables. From then on convalescence was rapid; there was a gain in weight of 11 lb. in the 22 days following the first esophagoscopy, and a marked gain in strength. The patient was allowed up and about the ward, and was discharged home on September 30, with instructions to return for further dilatation to maintain and increase the esophageal lumen. X-ray examination (Fig. 2) at the time of discharge was reported by Dr. Lingley as follows: "The stricture in the lower third of the esophagus has diminished in length and the lumen has definitely increased since the last observation. Barium now passes with only slight delay."

Esophageal stenosis as a complication of peptic ulcer of the stomach or duodenum has been reported by Vinson[1] and C. L. Jackson.[2] The coexistence of peptic ulcer of the esophagus and gastric or duodenal ulcer has also been reported (Abel,[3] C. Jackson,[4] and Friedenwald, Feldman

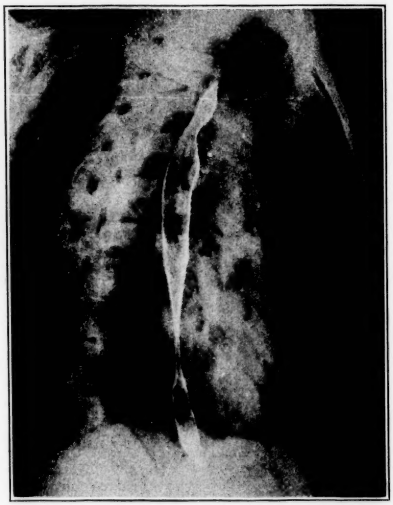

Figure 2. *X-ray of the esophagus after treatment, showing free passage of barium through the stricture.*

and Zinn[5]). In the case reported here no esophageal ulcer was demonstrable. In a study of 40 cases of cicatricial benign stricture of the esophagus of unknown origin Vinson reports 2 cases associated with duodenal ulcer. In C. L.

*At the last examination a piece of tissue appeared to be lying free in the lumen of the esophagus at the site of the stricture. This was removed with forceps for pathological examination. The report was "cellular exudate."

Jackson's report of 3 cases of esophageal stenosis associated with ulcer of the stomach and duodenum, 2 showed esophageal ulceration and 1 showed benign organic stenosis without peptic ulcer of the esophagus. The absence of substernal pain in our patient and the appearance of the esophagus by x-ray and by esophagoscopy make it probable that we were dealing with a benign cicatricial stenosis following acute esophagitis. Guisez, quoted by Friedenwald, Feldman and Zinn,[5] is convinced that many of the so-called simple ulcers of the esophagus are actually only localized inflammatory processes which finally terminate in stenosis without undergoing definite ulceration. As to the cause of the esophagitis in this case and the few similar ones reported, vomiting or regurgitation of acid gastric secretions may be of importance. Infection of the esophagus from the gastric or duodenal ulcer either directly or through the lymphatics may be a factor. The general nutritional state of the patient may also play a part. Bartels,[6] in a pathological and clinical study of 82 cases of acute ulcerative esophagitis, found gastric contents in the esophagus in all cases at necropsy. He did not discuss peptic ulcer of the esophagus, but esophagitis with phlegmonous or superficial ulcerations and erosions. In his opinion:

> It seems imperative that the action of the gastric juice be accepted as contributing to the lesion, because gastric juice was present uniformly in the lower third of the esophagus. Vomiting and even nausea without vomiting, with relaxation of the cardiac spasm, seem extremely important as factors that permit gastric juice to come in contact with the esophagus. It seems necessary that the patient should be debilitated, but not necessarily dying, before changes can occur in the esophagus. Debilitating and terminal states imply slowing of the circulation of the lower part of the esophagus, which normally is poor, and therefore loss of the normal resistance of esophageal tissue to trauma, and of its ability to regenerate.

In our patient vomiting was not a prominent symptom either before or after operation, although there were high jejunal obstruction, gastric distention, and probable regurgitation of gastric secretions into the lower end of the esophagus. Debilitation, however, was very marked. As to the etiologic importance of an in-lying gastric catheter, we do not believe it to be a factor, as it is so commonly used before and after gastric surgery without untoward results. In this connection Bartels concluded that passage of a tube is not an etiologic factor and may only incidentally be an aggravating one.

Symptomatically such patients may exhibit gas, substernal or epigastric distress, heartburn, nausea, regurgitation or vomiting, but as the esophageal lumen becomes narrow the outstanding symptom is difficulty in swallowing solid foods, and later with almost complete stenosis there is regurgitation of liquids. The diagnosis is easily made by x-ray and esophagoscopy.

The treatment should be esophagoscopy under local anesthesia, with bouginage under direct vision through the esophagoscope. Local anesthesia is used because general anesthesia is not only unnecessary but also dangerous in debilitated patients. Bouginage should be carried out under ocular guidance through the esophagoscope because, as Jackson and Jackson[7] have repeatedly emphasized, "blind bouginage should be discarded as an obsolete and very dangerous procedure."

SUMMARY

A case of benign stricture of the esophagus, probably due to an acute esophagitis following gastric resection for duodenal ulcer, is reported.

The etiology, symptomatology, diagnosis and treatment are briefly discussed.

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HYPERVENTILATION TETANY

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PROLONGED hyperventilation, whether practiced voluntarily in the laboratory or occurring as the result of some pathologic state, produces certain physicochemical changes that lead to tetany. The earliest observations on this subject were made between 1908 and 1912, when Haldane and Poulton,[1] Henderson,[2] Edsall[3] and others found that during experiments on hyperventilation their subjects complained of dizziness, tingling of the fingers and toes, and rigidity of the hands. In 1920, Collip and Backus[4] and, independently, Grant and Goldman[5] confirmed these findings and recognized the symptoms as those of tetany. Two years later, clinical reports of tetany caused by hyperventilation first appeared.[6, 7] Since that time there have been numerous case reports and considerable experimental work on the subject. In this paper the clinical syndrome will be discussed and some illustrative cases will be presented. But first it is necessary to outline the important chemical and physiologic changes produced by hyperventilation.

PHYSIOLOGY

Forced respiration causes a sharp drop in the carbon-dioxide tension of alveolar air.[1, 4, 5] As a result, an increased amount of carbon dioxide is washed out of the blood, and there is a drop in the carbon-dioxide content of the plasma.[4, 5] An increase in the pH of the plasma and a state of alkalosis accompany this change. At the same time there is an increase in the pH of the urine and a suppression of the output of urinary ammonia. These alterations in acid-base equilibrium have been constantly recorded in investigations on hyperventilation. Numerous other changes have been reported. Some observers have noted a slight increase in the concentration of serum calcium,[4] while others have noted no change.[8, 9] A marked drop in the concentration of serum inorganic phosphorus has been noted.[8] Several investigators have observed a rise in concentration of blood chlorides,[10, 11] and others have noted a decreased concentration of blood sodium.[12] Acetone frequently appears in the urine.[8, 10] In one experiment[13] a drop in cerebrospinal fluid calcium was reported, but this finding was not confirmed by other investigators.[9, 14]

In addition to the alterations in blood chemistry, various other phenomena have been observed. A period of involuntary apnea[2] frequently follows a period of forced respiration. Breathing is not resumed until the level of plasma carbon dioxide has risen to the point where the respiratory center is stimulated. A diuresis often follows hyperventilation.[4] There is usually noted a drop in systolic and diastolic blood pressures.[15] The pulse rate is increased. Experiments on dogs indicate that there is no attendant depression of the circulation.[16] The changes in the electrocardiogram are very slight; most observers report that the R waves and T waves have a smaller amplitude during forced breathing.[17] Several phenomena appear which are common to this and other types of tetany. There is an increased electrical excitability of peripheral nerves.[18] Chvostek's sign and Trousseau's sign are regularly present.

Although it is not my purpose to discuss the pathogenesis of hyperventilation tetany, some comment on the blood chemistry is pertinent from the therapeutic standpoint. Attacks of this type of tetany can be stopped by the administration of 5 per cent carbon-dioxide inhalations, by rebreathing and by the patient's holding his breath. All these have the effect of raising the carbon-dioxide content of the plasma, and thus simply reverse the changes produced by hyperventilation. Similarly, the administration of ammonium chloride, which decreases the pH of the blood without necessarily altering the carbon-dioxide content, tends to prevent hyperventilation tetany. Finally, attacks of this type of tetany have been immediately aborted by the intravenous injection of a calcium salt more alkaline than the blood.[13] It is thus possible that the decreased carbon-dioxide content and the increased pH of the plasma in hyperventilation produce some change in the blood calcium which causes tetany.

CLINICAL CONSIDERATIONS

Hyperventilation is seen in a wide variety of clinical conditions. Among the neurologic disorders it is seen most frequently in encephalitis lethargica.[6] Hyperventilation is not an uncommon response to pain,[7] and is occasionally seen during ether anesthesia.[19] Shannon[20] has produced evidence that, in certain cases, tetany of the newborn is due to hyperventilation. In cases of alkalosis of other origin, a slight amount of hyperventilation may precipitate an attack of tetany.[11]

Hyperventilation tetany is frequently seen in

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pregnant women.[21] In this connection it is interesting to note that there is normally an increased pulmonary ventilation and a decreased carbon-dioxide content of the plasma during pregnancy. However, the casual relation of these facts has not been definitely established.[22, 23]

By far the largest number of reported cases of hyperventilation fall in the group of psychoneuroses. Of these, anxiety neurosis and hysteria[24] appear to be the commonest, but hyperventilation is also a frequent response to rage, sorrow, fatigue, excitement and apprehension. Tetany has occurred during operations under local anesthesia,[25] after attacks of asthma[26] and after athletic events.[8] A more complete review of the literature would doubtless disclose many other factors which have precipitated tetany. The references cited here are given merely to show how frequently and under what varied circumstances hyperventilation and tetany may occur.

SYMPTOMATOLOGY

There is considerable variation in the symptoms reported by patients and laboratory workers suffering from hyperventilation tetany. Most patients complain first of dizziness, accompanied by numbness and tingling of the fingers and toes. Blurring of vision and tightness in the throat are frequently noted. There may follow difficulty in speaking, tightness across the upper chest or over the precordium, and spasm of the hands and feet. Twitching of the facial muscles may also occur. In very severe cases laryngeal stridor, generalized convulsions, opisthotonos and unconsciousness may occur. Usually, however, the tetany does not progress beyond the point where spasm of the hands appears. In many cases malaise, weakness and helplessness are prominent features. The patient falls to the ground as if in a faint, but consciousness is clouded little or not at all. Occasionally the patient becomes very frightened and has a feeling of impending death. Some patients learn from oft-repeated attacks that there is nothing to fear.

In any individual case, it will be found that many of the symptoms outlined above are not present, but almost without exception numbness and tingling and a certain amount of malaise or dizziness are present. Attacks vary greatly in duration, lasting from a few minutes to several hours. As the symptoms subside, the patient notices a physical and nervous fatigue which is proportional to the severity of the attack, and which may last for several days.

DIAGNOSIS

The diagnosis is not difficult. In most cases the increased rate or depth of respiration is obvious. There is a striking absence of the signs of cardiac or pulmonary disease. Chvostek's sign and Trousseau's sign are present, and the patient may exhibit typical carpopedal spasm. In certain cases, however, the hyperventilation is not at all obvious. A patient may have very slightly increased ventilation over a long period of time, and develop tetany without any marked increase in respiration. Or a patient may not be observed until the attack is subsiding and hyperventilation has ceased. In either of these cases a diagnosis of hyperventilation tetany may be confirmed by asking the patient to overbreathe vigorously for a few minutes. The patient reports a rapid return of symptoms identical with the symptoms of the attack, and the signs of tetany become apparent much sooner than would be expected in a person whose acid-base balance had not previously been disturbed. This test is quite harmless. Besides establishing the diagnosis, it is a dramatic way of pointing out to the patient the source of his trouble.

Several other conditions should be excluded. In the first place, tetany due to low serum calcium is to be considered. If the serum calcium is normal, tetany due to rickets, osteomalacia, hypoparathyroidism, steatorrhea and renal failure may be ruled out. Secondly, alkalosis from other causes should be considered, since tetany may occur after repeated vomiting and after excessive ingestion of alkalies. Finally, the possibility that the hyperventilation is due to a lesion in the brain must be recognized.

CASE REPORTS

Case 1 (M. G. H. No. 341569). R. P., a 21-year-old, single, white woman, was admitted to the hospital in October, 1934, complaining of intermittent attacks of weakness and collapse. She had been perfectly well until 1931, when she had had her first attack. This started suddenly, with dizziness, blurring of vision and frontal headache. She felt weak in the arms and legs, and noted numbness and tingling in the fingers and toes. The weakness progressed until, no longer able to stand, she fell to the ground crying uncontrollably. She remained fully conscious, but found that she was unable to speak, attempts to do so bringing forth only unintelligible sounds. Gradually her symptoms subsided, her vision cleared, and the numbness and tingling disappeared. She remained weak for several hours, and complained of extreme muscular fatigue.

After this first episode, the patient had similar attacks at irregular intervals, varying from 2 weeks to 3 months. The duration of attacks ranged from 10 minutes to 1½ hours. Attacks usually occurred at times of excitement or during emotional upsets. On two occasions the patient collapsed while swimming. At no time was there any loss of consciousness, convulsions or incontinence. Between attacks she felt well, and there were no other symptoms. Her past history and family history were negative.

Physical examination was essentially normal. The blood pressure was 132/88. A neurological examination was negative. Routine examinations of the blood and urine were within normal limits. The spinal fluid contained

50 red blood cells per cu. mm. and a protein of 51 mg. per cent. The basal metabolic rate was —4 per cent. X-ray of the skull was negative.

The patient had an attack a few minutes after the metabolism test was completed. She complained of weakness, malaise and tingling in the fingers and toes. She began crying in a hysterical fashion and was soon unable to speak, although she was able to understand questions and to answer by shaking her head or nodding. During this attack her color was good. She was very restless, and threw herself about on the bed, crying constantly. Her respirations were markedly increased. The blood pressure was 160/110, and the pulse 90. Chvostek's sign was present, and Trousseau's sign was elicited 20 seconds after applying the tourniquet. The patient's condition remained unchanged for 30 minutes. At the end of this time venous blood was removed for analysis, and she was given 10 cc. of a 10 per cent solution of calcium gluconate intravenously. She experienced immediate symptomatic relief. The venous blood sugar was 101 mg. per cent. The serum calcium was 11.0 mg., and the serum phosphorus 2.2 mg. per cent. On the following day the serum calcium was 10.2 mg., and the phosphorus 4.0 mg. per cent.

Further studies on this patient revealed that she reacted to any emotional situation by increased rate and depth of respiration. Excitement of any sort, pleasant or otherwise, provoked the response of hyperventilation. Except for this type of response and a tendency to become easily excited, she appeared well balanced. She gave the impression of being genuinely eager to be cured.

The treatment consisted simply of an explanation of the mechanism of her attacks. To illustrate the validity of this explanation she was asked to breathe rapidly for a short period. A typical attack was thus induced in 6 minutes. A paper bag was then placed over her head and secured loosely about the neck. She continued to breathe rapidly, but her symptoms subsided in a few minutes.

The patient was discharged with instructions to observe and control her breathing, especially in moments of stress, and to hold her breath or re-breathe into a paper bag if an attack occurred. Three years later (October, 1937) she wrote to say that she had had no further severe attacks. She had continued to have occasional tingling of the hands, but had been able to prevent the development of further symptoms by holding her breath.

*Case 2.** Mrs. J. W., a 54-year-old housewife, had suffered from intermittent attacks of collapse since the age of 23. These attacks varied greatly in duration and intensity, but a typical seizure was as follows. There was a sudden onset of extreme fatigue and depression, and the patient felt like lying down at once. This was quickly followed by blurring of vision, and numbness and tingling of the hands and feet. A sudden weakness of the legs caused her to collapse on the floor, where she lay fully conscious but unable to move or speak. At the same time she noted a sense of pressure on the upper part of her chest, and complained of a smothering sensation which caused her to gasp. As the symptoms subsided she felt little desire to breathe at all. After the attack the patient felt very weak, and was quite fatigued for several days.

Similar attacks occurred on an average of every 3 months, although occasionally the patient was symptom-free for nearly a year. Recently attacks had become increasingly frequent and severe, and varied in duration from 30 minutes to 5 hours. On one occasion a doctor observed spasm of the hands. It was frequently noted that her pulse was feeble and her breathing was irregular. At the height of one attack her respirations ceased altogether for several minutes. When her symptoms were particularly severe she appeared to be "practically unconscious," and retained only a vague recollection of the episode. On several occasions a marked diuresis followed an attack.

The family history and past history were negative. At the age of 28 a cholecystectomy was performed. At 33 a small uterine fibroid and the appendix were removed. After this operation the surgeon told her that she had taken the ether "very badly" and warned her against further anesthesia.

Between attacks the patient enjoyed robust good health. She played golf regularly and was active in social affairs. Her obvious well-being in these intervals, coupled with the apparent seriousness of her attacks, puzzled her physicians. The patient noted that her attacks always followed a period of unusual activity or emotional stress; it was when her social calendar had been particularly full that she succumbed. She gave the impression of being calm, well adjusted and energetic.

On April 28, 1936, the patient had a typical attack in my office. Suddenly complaining of dizziness and tingling of the hands, she threw herself on the couch as though completely exhausted. Her color was good. She was breathing deeply at the rate of 30 respirations per minute. The pulse was 90 and of good quality. The blood pressure was 140/90. The heart sounds were normal, and the lungs were clear. Chvostek's sign was present, and Trousseau's sign was elicited in 40 seconds. The patient was instructed to hold her breath. She did this for 2 minutes without apparent difficulty and noted that her symptoms abated considerably. She was then asked to breathe rapidly. Her symptoms quickly returned, but again subsided after a paper bag had been placed over her head.

On the following day she still complained of fatigue, but had no other symptom. The blood sugar was 103 mg. per cent, and the serum calcium 9.7 mg. She was discharged with instructions for regulating her breathing. For 18 months she had no severe attack, although occasionally the warning symptoms of fatigue and blurring of vision occurred. In October, 1937, she had a fairly severe attack, following several weeks of overactivity and nervous strain.

Cases 1 and 2 are nearly identical in that hyperventilation was a constant and unconscious response to emotional stimuli and fatigue. Severe attacks of collapse occurred irregularly over a period of years, and interfered to a considerable extent with activity. In neither case was there an obvious neurotic background to the overbreathing. In Case 1 the attacks ceased when the method of preventing them had been explained to the patient. In Case 2 there was only one severe attack in the subsequent eighteen months. It is apparent, however, that neither patient became sufficiently aware of the importance of hyperventilation. The transient episodes of dizziness and tingling of the extremities, occurring under circumstances that previously had preceded a major attack, indicated that these patients continued to respond to certain situations by overbreathing.

*The author is indebted to Dr. Roy R. Wheeler for permission to publish the report of this case.

Case 3 (M. G. H. No. 55942). N. F., a 17-year-old boy, was referred to the Out Patient Department of the Massachusetts General Hospital with a diagnosis of tetany due to overventilation. Six months before admission he began having attacks of severe precordial pain accompanied by dizziness, sweating, numbness and tingling of the hands, spasm of the hands, twitching of the face and shortness of breath. The attacks lasted from 30 minutes to 2 hours, and left him with a sense of extreme weakness and fatigue. Attacks occurred almost daily, and were of such severity that his doctor advised complete bed rest. His attacks continued unabated. The patient developed a constant precordial ache, which became a sharp constricting pain during the attacks of spasm. Temporary relief was afforded by the intravenous injection of a solution of calcium levulinate. Later the patient was given calcium salts and ammonium chloride by mouth, and spasm of the hands no longer occurred during attacks. Otherwise his condition remained unchanged.

The family history and past history were negative. At physical examination the patient was well developed and appeared healthy. He was extremely nervous and tense, and was unable to sit quietly. He was breathing deeply and rapidly, because he felt "short of breath, unable to get a deep breath." The heart and lungs were normal. The blood pressure was 160/80. The pulse was 120. The knee jerks were hyperactive. Chvostek's sign was present, and Trousseau's sign was quickly obtained. The urine was neutral to litmus, and normal in other respects. The serum calcium was 11.0 mg. per cent, and the serum phosphorus 2.42 mg. A blood Hinton test was negative.

The patient was asked to omit all medication and was given an explanation of his symptoms. He was advised to stop trying to get a deep breath, and to control his breathing at all times. One week later he returned to the clinic, and presented an entirely different appearance. He was calm and quiet. His blood pressure was 110/70. The pulse was 80. The tendon reflexes were normal. The signs of Chvostek and Trousseau could not be elicited. The patient had had no further attacks, and there had been no precordial ache. He stated that he had had no difficulty in controlling his breathing. In a letter 6 months later (November, 1937) the patient reported that he was still nervous at times, and suffered occasionally from shortness of breath, precordial pain and weakness. He had had no further attacks of carpal spasm.

The precipitating factor in this illness was a difficult family situation which apparently kept the patient in a state of tension that was reflected in his overbreathing. Anxiety about his condition and the precordial ache doubtless served to increase his hyperventilation once the state of tetany had been established. Although he derived some benefit from his visit to the clinic, his later course was determined more by his emotional conflict. In this case, as in Cases 1 and 2, the habit of overbreathing persisted, but was not so excessive as it had been. If these patients had been available for a thorough psychiatric investigation a more permanent and complete improvement might have been obtained.

In view of the variety of conditions in which hyperventilation tetany can occur, it is probable that it is much commoner than is indicated by a survey of the literature. That 2 of the cases reported above went undiagnosed for years is certainly an indication that the condition is not sufficiently understood by the practicing physician. The presence of carpal spasm undoubtedly points the way to a correct diagnosis in a large majority of cases. But in many instances, as shown in the 3 cases reported in this paper, incapacitating symptoms may develop in the absence of carpal spasm. Transient episodes of tingling of the extremities with a vague history of periodic attacks of collapse or "hysteria" should direct the physician's attention toward the possibility of hyperventilation. If an effort is made to see the patient during an attack, this possibility can be affirmed by the presence of the signs of tetany. Once the diagnosis has been made, it is possible to give the patient instruction in regard to proper breathing. In many instances he will learn to prevent the occurrence of further attacks.

SUMMARY

1. The chemical and physical changes occurring in hyperventilation tetany are briefly reviewed.

2. The clinical aspects of this condition are discussed.

3. Three cases in which frequent attacks of tetany resulted from overbreathing are presented. In each case, improvement resulted when the mechanism of the attacks had been explained, but the patients continued to respond to certain situations by increased ventilation.

6 Commonwealth Avenue.

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HENDEN HOSPI... CONN.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 24141

PRESENTATION OF CASE

A sixty-four-year-old, white, Italian barber entered the hospital with the complaints of anorexia and vomiting of two months' duration.

For twenty-five to thirty years before entry he had always had a poor appetite, and for the fifteen years before entry had had frequent attacks of nausea and vomiting. He was bothered greatly by gaseous distention and "gas pains," which came on directly after eating and were usually relieved by eructations. However, he frequently became nauseated and regurgitated or vomited the food he had eaten. The frequency of vomiting could not be determined, but it usually occurred after eating large amounts of food. Soda gave him no relief. He never vomited fresh or changed blood or passed tarry stools. For many years his bowels had been sluggish, and it had been necessary for him to take castor oil or other laxatives two or three times a week. If he did not take laxatives, his vomiting occurred more often.

About two months before entry he developed a dull, gnawing, aching sensation in his midepigastrium, which came on ten minutes to one and a half hours after eating and was usually relieved by vomiting. The aching sensation often radiated into both upper quadrants and occasionally through to the back. Gradually the vomiting changed to frank regurgitation of practically everything eaten or drunk. He was able to swallow successfully but could not lie down after meals because the food would "roll right out," practically in an unchanged state. During the two months before entry he had lost 22 lb. and had become very weak and pale.

For fifteen or twenty years before entry he had had a chronic cough productive of moderate amounts of yellowish sputum. Most of the sputum was raised in the morning. It was never foul or blood streaked. For two or three years before entry he had a sensation of a "little ball" tickling the back of his throat. He had had no night sweats or persistent fever. His past history was otherwise essentially negative, and his family history was not contributory.

Physical examination revealed a fairly well-developed man, showing evidence of considerable weight loss. The skin and mucous membranes were pale, and the tongue was heavily coated. The heart was negative, and the blood pressure was 110 systolic, 75 diastolic. At the right lung base posteriorly there were slight dullness and decreased tactile fremitus, voice sounds and breath sounds. Coarse rhonchi were heard in the right chest, which disappeared on coughing. There was an indefinite hard tender mass in the epigastrium just beneath the xiphoid, which was difficult to delineate because of spasm of the abdominal muscles. The mass seemed to extend into the right upper quadrant, and was thought possibly to be continuous with the liver. No definite liver edge could be felt and no other masses or spasm were made out. The rectal examination was negative.

The temperature was 97.5°F., the pulse 65. The respirations were 20.

The urine examination was negative. The blood showed a red-cell count of 4,500,000 with 65 per cent hemoglobin, and a white-cell count of 31,500 with 88 per cent polymorphonuclears. The sputum was yellowish in color and contained gram-positive diplococci. The vomitus contained particles of food and gave a negative guaiac test. Gastric lavage was attempted, and the fluid obtained contained no free or combined hydrochloric acid and gave a 2+ guaiac test. The blood Hinton and a 1:40,000 tuberculin test were negative. The nonprotein nitrogen of the blood was 45 mg. per cent.

Fluoroscopic x-ray examination of the chest revealed a large mass projecting to the right from the upper mediastinum. The lung fields were otherwise clear, and the diaphragm appeared normal. Barium given by mouth filled a tremendously dilated esophagus, and the previously observed mass was seen to represent the esophagus almost filling the right upper chest. The dilatation was greatest in the upper portion of the esophagus but was also marked throughout the lower half. No barium passed into the stomach during fifteen minutes of fluoroscopic examination.

On the day following entry his temperature rose to 100°F. and on the next day to 102°F. His respiratory rate increased to 35. Thorough lavage of the esophagus was done on several occasions and somewhat improved his condition. However, only very small amounts of fluid could get through the cardia. His temperature and respirations remained elevated, and on the sixth day definite signs of pneumonia could be made out at the right lung base. He died on the eighth day.

DIFFERENTIAL DIAGNOSIS

DR. CHESTER M. JONES: The story seems to me to present two possible diagnostic problems in addition to the obvious terminal pneumonia. In the first place we have a patient who has had for at

least fifteen years, and possibly twice that length of time, symptoms of esophageal obstruction with gradually increasing obstruction and gradual enlargement in the size of the esophagus. Anything that extends over such a period of time by itself cannot be considered a malignant lesion. Therefore, I should say that the symptoms and story were those of a benign obstructing lesion at the lower end of the esophagus. The x-rays show an enormous barium-filled tube that narrowed down in a funnel-shaped manner to the cardiac orifice. There is no mention in the x-ray report in the record that there is anything but a symmetrical or fusiform narrowing of the lower end of the esophagus. The mass that was first noted by x-ray might have been outside the esophagus or connected to it by a small opening. In other words, it might be a huge esophageal diverticulum under the right clavicle, filled with food and fluid, but it seems more reasonable to assume that the whole picture represents a tremendously enlarged esophagus. It is still possible that there was a diverticulum of the upper third; as a matter of fact the upper third is the weakest portion and does dilate readily if back pressure is put against it. So the x-ray findings fit perfectly well with an obstruction at the lower end of the esophagus and explain part of the clinical picture. I cannot conceive of this obstruction's having been due primarily to cancer at the cardiac end of the esophagus. Fifteen years of continuous symptoms without change in character would seem to indicate a benign process which was gradually increasing.

I suppose it is possible that this process could be a stricture due to previous trauma or to chemical injury following the ingestion of lye. It could be due to congenital narrowing of the lower end of the esophagus or a congenital hypertrophy of the cardiac end of the esophagus. These conditions do occur. We have seen as large an esophagus as this due to cardiospasm of many years' duration. I can recall one that had a story of at least twenty years' duration with a very large esophagus. They do not mention the actual content. I think the largest amount recorded is 1800 or 2000 cc. So far as the size of the dilated esophagus is concerned, any of these benign processes are possible causes, but they will not explain certain other findings. Obviously the man is dehydrated, undernourished and constipated because of lack of sufficient food. He is anemic because of malnutrition. His nonprotein nitrogen is elevated because of dehydration. The only unexplained laboratory finding is the leukocytosis of 31,000 with 88 per cent polymorphonuclears. That goes perfectly well with a pneumonic infection which is not obvious on these plates but is suggested by the admission chest signs, and we know that he subsequently died with a clinical picture of pneumonia.

We are left with a story of chronic cough and yellow sputum. He may have had bronchiectasis, but the x-ray findings do not suggest any such possibility. This chest plate is an oblique view. It does not suggest a bronchiectatic process to me, nor does it suggest any real pneumonic process. I am not going to consider the story of cough and sputum as related to the main part of the history.

Two months before entry he gives a story of something new — epigastric pain coming ten minutes to one and a half hours after meals, usually relieved by vomiting. Here again we may be dealing with an overdilated esophagus with a certain amount of irritation at the lower end which is relieved by regurgitation. This symptom, however, seems to have a different significance from that of the earlier symptoms.

We have a physical finding which I think is extremely important, that is, an indefinite, hard, tender mass in the epigastrium just below the tip of the xiphoid. That does not go with esophageal disease unless it represents metastases from tumor. I have not seen a sufficient number of cases of cancer of the esophagus to know where they tend to metastasize. I should expect them to metastasize to the mediastinal nodes rather than below the diaphragm. The mass may be associated with the liver, of course, or it may be the stomach, but it has to be one of these organs.

It is entirely possible that we have to make two diagnoses, one of a benign process which is more or less obstructing the esophagus and has done so increasingly over a period of many years, and then a second process which has changed the symptoms recently and at entry is associated with a mass at the tip of the xiphoid. It may represent cancer of the stomach or just outside the stomach and in the liver. I do not believe he has tuberculosis, but the negative 1:40,000 tuberculin test does not rule it in or out. It is of some interest that the Hinton test is negative. It says here "only very small amounts of fluid could get through the cardia." I do not feel at all sure that they knew where the tube was. It is possible it never went below the cardia, and it is also possible that they never entirely emptied the esophagus. I am wondering about the possibility of prolonged irritation at the lower end with possibly an inflammatory process with erosion and ulceration and an abscess below it, which might be the basis of this epigastric mass. The mass is tender, which is not like many malignant processes, but the patient did not come in with

the clinical signs of abscess formation. In other words, he did not come in with high temperature although he did have a leukocytosis. I think it is more logical to interpret the leukocytosis as going with something that is beginning to form in the right chest that subsequently became pneumonia. I am disturbed that there is nothing in the x-ray films interpreted as a pneumonic process at the right base; nevertheless, I believe he died of a terminal pneumonia. I am sure he had a stricture of the esophagus due to a very benign process. I do not believe it was due to esophageal ulcer, because he does not give a story of ulcer pain. I do not believe he has cancer of the esophagus as an explanation of the entire picture. The recent picture, plus the epigastric mass, I am inclined to explain on the basis of cancer. A malignant tumor in the stomach would be my first guess.

Dr. Francis M. Rackemann: Do you suppose he could have a rupture at the lower end, with abscess formation?

Dr. Jones: I mentioned that as a possibility. Of course if it involved that portion under the diaphragm he could get a localized abscess. I think that is a possibility.

Dr. James H. Means: Would ventral hernia give a picture like this, with recent cardiospasm at the upper end of the stomach?

Dr. Aubrey O. Hampton: This picture of the esophagus, the extreme dilatation and this spasm, is quite consistent with cardiospasm. The difficulty of ruling out any other lesion would be great because his esophagus is filled with food and these filling defects cannot be displaced by palpation or any other maneuver except lavage, and it apparently was not done during this examination. He did show this defect in the anterior aspect of the lower end of the esophagus which is present when he is lying down or standing. It does not materially shift or change. It is also strange that this portion of the esophagus is much smaller than the upper portion. I think that the peristaltic activity in the posterior aspect of the esophagus is more than you would expect in the presence of cardiospasm alone, and, furthermore, we do not see the same peristaltic waves in front. I do not see any evidence of perforation of the esophagus or of pneumonia. The diaphragm is perfectly normal in outline and position.

Dr. Jones: That was one thing I should have mentioned. If he had a perforation of the esophagus that caused a mass below the xiphoid you should have been able to see barium going through.

Dr. Hampton: I should think so. I do not believe he had a perforation at the time of this examination. We cannot reach a definite conclusion about this lesion, but it certainly looks like carcinoma.

Dr. Wyman Richardson: I saw this man in the Out Patient Department and sent him in with a diagnosis of carcinoma of the stomach. I do not know the answer now, but my diagnosis still holds. I disregarded the long history but wondered if he might not have had previously a diaphragmatic hernia of the stomach.

Dr. Hampton: I have never seen dilatation of the esophagus to that degree due to carcinoma. That is an enormous esophagus.

Dr. Means: Do you ever see an esophagus of that size due to diaphragmatic hernia?

Dr. Hampton: No; I do not believe it would become that large, even with an ulcer at the lower end or a benign stricture.

Dr. Edward B. Benedict: I have never seen an esophagus of that size except in cardiospasm.

Clinical Diagnoses

Cardiospasm with esophageal dilatation.
Bronchiectasis.

Dr. Jones's Diagnoses

Benign esophageal stricture (chronic).
Cancer (probably of stomach).

Anatomical Diagnoses

Dilatation and muscular hypertrophy of esophagus (cardiospasm).
Carcinoma of esophagus with metastases.
Abscess in subdiaphragmatic metastasis.
Acute pneumonitis with abscess formation.
Pulmonary tuberculosis, healed, apical.
Arteriosclerosis, generalized, moderate.

Pathological Discussion

Dr. Tracy B. Mallory: The autopsy on this man showed, of course, an enormously dilated esophagus with a frank tumor mass at its lower end, chiefly anterior, but to some extent encircling the esophagus and extending down into the stomach for a short distance. There was also a large tumor mass beneath the diaphragm, lying just anterior to the cardia of the stomach and medial to the spleen; this mass consisted of tumor tissue with a large central abscess cavity and a fistula from this cavity into the esophagus. It seemed to be on the point of rupture into the lesser peritoneal cavity but that had not occurred. The tracheal nodes showed metastases and were very much enlarged. It was obvious that the carina was flattened a good deal. There were metastases to the liver, kidneys and a few other lymph nodes. The

tumor was a squamous-cell carcinoma, obviously primary in the esophagus.

I should agree entirely with Dr. Jones's discussion, though I cannot prove his contention by any anatomical facts. I do not believe a carcinoma of the stomach can give rise to as large an esophagus as this. I think he must have had some form of benign stricture — almost certainly cardiospasm — for years and that the carcinoma was a relatively late, terminal complication.

There was one other finding; at the right base there was pneumonic consolidation with many abscess cavities within the consolidated area, so that the "pneumonia" without much question was really an inhalation pneumonitis from regurgitation and aspiration of material from the esophagus. That is not an uncommon complication in esophageal stricture.

DR. HAMPTON: His chest plates ought to have shown bronchopneumonia at both bases, but they are strangely clear.

DR. JONES: What is the usual spread of carcinoma of the esophagus below the diaphragm?

DR. MALLORY: A fair number will extend across the sphincter and actually invade the stomach for a short distance. The most common spread is to the regional nodes and frequently there is direct extension to the pleura and lungs.

DR. RACKEMANN: Did the tumor extend upward far enough to account for the defect in the wall of the esophagus?

DR. MALLORY: Yes.

DR. RICHARDSON: Is there not a definite inflammation of the esophageal wall in cardiospasm?

DR. MALLORY: One can say that the esophageal wall above the tumor is quite hypertrophied in spite of the dilatation. It still is much thicker than a normal esophagus, which would prove anatomically that the obstruction was of long duration, at any rate much longer than the few months of the terminal part of the history. So far as any other specific lesion of cardiospasm is concerned, I am not convinced there is one.

DR. JONES: In the ones you have examined do you not find a narrow cardiac orifice with fibrosis?

DR. MALLORY: There is always some fibrosis: anyone who has retained food in the esophagus for twenty years should have a little inflammatory reaction to it.

CASE 24142

PRESENTATION OF CASE

First Admission: A fifty-five-year-old housewife entered the hospital with the complaint of difficulty in swallowing.

She felt perfectly well until seven months before entry, when she began to have pain in her epigastrium brought on by swallowing solid food. As soon as the food passed a certain point in her esophagus the pain ceased. She was perfectly comfortable when not swallowing. These symptoms continued and became slightly more troublesome until four months before entry, when for a period of two weeks she had a remission and was able to swallow solid foods without difficulty. However, her symptoms returned and for the two months before entry she was able to eat only semi-solid foods and liquids. During the week before entry she even began to have difficulty in swallowing liquids. During her illness she lost at least 20 lb. in weight. She had had no nausea, vomiting, hematemesis or melena. Her past history and family history were noncontributory.

Physical examination revealed a well-developed, somewhat emaciated white woman, in no apparent discomfort. Except for emaciation and dental caries, the physical examination was entirely negative. The blood pressure was 106 systolic, 76 diastolic.

The temperature was 98.6°F., the pulse 95. The respirations were 20.

The urine examination was negative. The blood showed a hemoglobin of 75 per cent and a white-cell count of 7100 with 66 per cent polymorphonuclears. The blood Hinton test was negative.

An x-ray examination of the esophagus showed a tumor mass infiltrating the right side of the esophagus in its lower third. The tumor caused marked narrowing of the lumen so that the barium stream was reduced to a trickle and passed very slowly into the stomach. The esophagus above the lesion was dilated and showed marked peristalsis. The stomach was normal.

She stayed in the hospital for three months and was given daily x-ray treatments amounting to 11,600 r. units. The radiation was given in doses of 200 r. through four portals. She was fed by nasal tube for the first two months and was fairly comfortable except for occasional nausea and rare episodes of vomiting. On one occasion she vomited about 100 cc. of thin red fluid. After the first two months the tube was removed, and she began taking fluids and soft solids with little difficulty and no pain. Three weeks later an x-ray examination of the esophagus showed no definite lesion. She continued to improve and gain weight, and a week before discharge a repeat x-ray examination again showed an apparently normal esophagus. There was slight thickening of the upper part of the stomach in the posterior wall, but there was no evidence of tumor.

Final Admission (three months later). For about six weeks after discharge she had only very slight difficulty in swallowing, but she developed a dull, constant, aching sensation across the upper part of her abdomen. She also had a poor appetite but no other symptoms. One month before re-entry she again began to have severe dysphagia with regurgitation of almost all solids and liquids. Finally she was practically unable to take anything by mouth and was given rectal feedings. She had lost about 15 lb. in weight during the month before re-entry.

Physical examination revealed a cachectic woman, obviously very ill. Her blood pressure was 85 systolic, 65 diastolic. The examination was otherwise essentially negative.

On the day of entry an operation was performed.

Differential Diagnosis

Dr. Earle M. Chapman: The problem here is obviously the diagnosis of a mass which is causing an infiltrating type of lesion in the lower third of the esophagus, particularly on the right side. The record says, "The tumor mass caused marked narrowing of the lumen so that the barium stream was reduced to a trickle and passed very slowly into the stomach." So we know there is a mass obstructing the esophagus. One interesting point is that she first had difficulty in swallowing solid foods, later liquids. It also says that for two weeks she had a remission and was able to swallow solid foods without difficulty. That to me is rather surprising and I am at a loss to explain it. I do not know why in the course of this disease she should suddenly be free of symptoms. One thinks of unusual lesions, such as a polyp which might lie in the esophagus and move or change in position. I do not see how autodigestion could occur while it was in the esophagus, but if it were on a long pedicle and reached into the stomach, that is possible. One thinks of metastases or some process forming an abscess cavity that drained into the esophagus. There is nothing to indicate that it drained into the pleural space or into the lung. I think these are remote possibilities of what might have explained the remission. The x-rays are the most important part of the whole examination. Perhaps Dr. Hampton will show them.

X-Ray Interpretation

Dr. Aubrey O. Hampton: These three films were taken at the first examination; we have an examination nearly three months later and another four months after the second. The total time between the first and last examinations is seven months. The first examination was before irradiation and shows this filling defect at the lower end of the esophagus with dilatation above, which is quite consistent with carcinoma of the esophagus. Then twenty-seven days later, following irradiation, the esophagus is, so far as I can tell, perfectly normal. I do not believe anyone would suspect that the stomach is abnormal.

Dr. Chapman: What do you mean by "thickening of the upper part of the stomach in the posterior wall, but no evidence of tumor"?

Dr. Hampton: It appears straight and rather rigid at that point, but I should not make a diagnosis of intrinsic disease. But four months later there is definite irregularity of the stomach in the same area that was suspected of being abnormal before, and the irregularity in the lower end of the esophagus is of the same general appearance as before x-ray treatment, except that there is less obstruction. In the upright film taken of the abdomen you can see a gas bubble in the fundus of the stomach, which outlines a definite intrinsic filling defect.

Differential Diagnosis (continued)

Dr. Chapman: What is this tumor mass? We know it is there. What is its character? It is obvious to me that carcinoma was diagnosed clinically. It is characteristic of carcinoma from the x-ray finding, and the story is that of carcinoma. Another fact is that she was treated as if she had carcinoma. She received 11,000 r. which is the dose given for carcinoma. It did respond to treatment. It would be interesting to know what the esophagus and the mucous membrane showed following such a massive dose of x-ray. It was wise I suppose that a tube was put down during the treatment, because with that amount of treatment over a tumor area she might have perforated and developed mediastinitis if she were allowed to swallow. The fact that she had a tube in place was a precautionary measure. To me, the facts that she had slight thickening of the upper part of the stomach in the posterior wall, and that this disease started higher up in the esophagus and spread down into the stomach, suggest that the lesion was not a carcinoma. The fact that it does not produce great irritation in the lining of the stomach also points to a different type of lesion. It suggests lymphoblastoma of some sort. What type could it be? Hodgkin's disease is extremely rare in the esophagus. I know of one case, however, because I was fooled on it at a similar conference with third-year students. I said on that occasion: "Hodgkin's is one type of lymphoblastoma that I

have never seen involving the esophagus." But that is what it was.

What other type could this be? Perhaps the diffuse, spreading type of lymphosarcoma. We also see diffuse spread of the reticulum-cell and stem-cell types. We know that she responded to x-ray, but the response is no proof of the diagnosis. If this were any form of lymphoblastoma she probably would have responded to a much smaller dose of x-ray. On the other hand the fact that she shows this picture is very suggestive of lymphoblastoma.

As to the final episode when she returned, examination was again negative. I am surprised that physical examination did not show some enlargement of nodes in the neck, groin or retroperitoneal region, or possibly a palpable or enlarged spleen. Her blood pressure had fallen, but I believe we need not think of a cardiovascular accident, such as coronary occlusion. I should think that lymphoblastoma is a good working diagnosis, and it is the best I can offer.

Clinical Diagnosis

Lymphoblastoma of the esophagus.

Dr. Chapman's Diagnosis

Lymphoblastoma of the esophagus and stomach, probably lymphosarcoma.

Anatomical Diagnoses

Carcinoma of esophagus with extension to stomach and metastases.
Esophagopericardial fistula.
Pericarditis, acute fibrinopurulent.
Empyema, right.
Pulmonary infarct.
Operative wound: gastrostomy.
Cholecystitis, chronic.
Cholelithiasis.

Pathological Discussion

Dr. Tracy B. Mallory: With any tumor in this area I think it is impossible to distinguish clinically whether it starts in the stomach or esophagus. X-ray examination may be misleading, and sometimes it is even impossible at autopsy. Histologic examination usually settles the issue, but once in a while it is difficult even when all the facts are in. I think I should explain why such a massive dose of x-ray treatment was given to this patient. A biopsy was done and on a section which was sent to us from another laboratory we found obviously malignant tumor cells, predominantly spindle-shaped, and we made a diagnosis of leiomyosarcoma. That is not a radiosensitive tumor, and our report undoubtedly influenced the x-ray department to use the maximum dose. They were then quite astonished to see the disease melt away. If it really had been a leiomyosarcoma even after such a dose it probably would not have been affected. The tumor, as you have seen, recurred fairly promptly, and at the time of autopsy we found a large tumor involving both the lower end of the esophagus and the cardia of the stomach. There was ulcerated tumor extending 4 cm. above the cardia, and a fungating mass which extended down into the stomach for 6 or 7 cm. The tumor had grown through the posterior wall of the stomach and was invading the pancreas. There was a perforation through the esophageal portion of the tumor into the pericardium, with a terminal pericarditis. There was also an empyema. We could not discover any fistulous tract connecting the esophagus and the empyema. On microscopic examination it was quite evident that it was an epidermoid carcinoma which must have been primary in the esophagus. It was of a very high grade of malignancy. These very undifferentiated epidermoids are fairly sensitive to radiation, and the temporary response is therefore not surprising.

*SECTION TWO**

EDITORIAL

THE COMMISSIONER OF PUBLIC HEALTH

THE functions of the Massachusetts Department of Public Health are many. Its Division of Communicable Diseases, through the district health officers, assists local boards of health in the control of disease, and offers diagnostic aid through the Bacteriological Laboratory at the State House. Its Division of Biological Laboratories manufactures and supplies various biological products for the treatment of disease, and gives diagnostic aid through the Wassermann Laboratory. Its Division of Food and Drugs protects the people of the Commonwealth against the adulteration of food and drugs. Its Division of Tuberculosis is in charge of the state sanatoriums that care for the tuberculous and those with cancer and the sequelae of infantile paralysis, in addition to conducting the tuberculosis-control program and the follow-up work in connection with the Chadwick Clinics. Its Division of Child Hygiene is concerned with all aspects of child health. Its Division of Adult Hygiene conducts investigative and educational work in regard to cancer, diabetes and arthritis. The work of its Division of Genitoinfectious Diseases is largely educational, but this division also subsidizes a number of municipal clinics for the treatment of gonorrhea and syphilis. Its Division of Sanitary Engineering has oversight of water supplies, sewage-disposal systems and the shell-fish industry; certain special engineering projects are carried through each year, and the division conducts an Experiment Station, which has made many important contributions to our knowledge of sanitary engineering. Its Division of Administration, in addition to supervising the activities of all other divisions and to directing general public-health problems, has charge of the crippled-children's clinics which are financed through grants from the United States Public Health Service and the Children's Bureau.

During 1937 over $3,200,000 was required to finance all these activities, in addition to federal grants under the Social Security Act of approximately $400,000. The department employs nearly 1500 individuals, and during the past year furnished 387,000 days of state-sanatorium care to 1900 patients, in addition to that required by 1437 persons admitted to the Pondville Hospital.

The responsibility of directing this huge undertaking rests upon the Commissioner of Public Health, and the people, particularly the physicians, of the Commonwealth have every right to demand that he be experienced and of proved ability, as specified by existing statutes.† Beliefs, political or otherwise, should not influence his selection: the health of the people is far too important to be jeopardized by such considerations, as has been amply demonstrated by the unfortunate series of events in the Department of Mental Diseases during the past two years.

If the excellence of and the notable contributions to public-health administration that have characterized the activities of the Massachusetts Department of Public Health for nearly seventy years are to continue, this department must be under the guidance of one who has had special training and experience in public-health work. The Council of the Massachusetts Medical Society at its stated meeting on February 2 passed a resolution approving of Dr. Henry D. Chadwick's reappointment. *It becomes the duty of all members of the Society to make every possible effort to effect his continuance in office!*

*This issue of the *New England Journal of Medicine* is published in two sections.

†*General Laws*, Tercentenary Edition, Chapter 17, Section 2.

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U.S.P. UNITS FOR LIVER EXTRACT

With the preparation of the first extracts of liver for use in pernicious anemia it became apparent that variable losses of potent material occurred, depending on the method of manufacture. Nevertheless, until quite recently, in describing such products reference has usually been made to the amount of liver used in their preparation rather than to the potency of the final product.

The first step toward a better definition was taken a few years ago by the Council on Pharmacy and Chemistry of the American Medical Association, which established for acceptable products certain minimal requirements in terms of hematopoietic power when given in reasonable dosage. With the eleventh revision of the *Pharmacopoeia of the United States,* the determination of the potency of preparations of liver or stomach was referred to the Anti-anemia Preparations Advisory Board. To this board, various manufacturers have submitted data as to the clinical effectiveness of certain preparations of liver administered in a specified manner, and from these data the board has assigned a unitage to each product. Elsewhere in this issue will be found a definition of the meaning of these units, whether for "oral" or for "injectable" products, together with a list of values in terms of units for each preparation at present accepted.

It is to be emphasized that, although a unit of material prepared by different manufacturers may be expected to produce similar hematopoietic effects in pernicious anemia, it is not known that units of all preparations will have similar effects on gastrointestinal and neural manifestations. There is some evidence to suggest that even the hematopoietic effect of preparations of liver depends on multiple factors rather than a single chemical entity; and it is possible that with different manufacturing processes variable amounts of substances with a particular effectiveness, respectively, on the gastrointestinal and the neural manifestations of pernicious anemia have been retained. Such differences are perhaps especially likely to appear in the treatment of atypical patients or in related conditions such as sprue or the pernicious anemia of pregnancy.

The number of products accepted by the board means that no physician need use products not so listed. Although certain eminently satisfactory products do not appear in the present list, the board expects to assign unitage to new products which may be submitted; it will also re-evaluate products according to new clinical data. By comparison of the unitage, the relative concentration and the bulk of these products, the physician should be able to select the preparation most suitable for his purpose. With a knowledge of the price of the various preparations he should be able to estimate the comparative cost per unit of potency of different preparations. At any rate, an important step in the right direction has been taken in that the medical profession now has available a better knowledge of the potency residing in the final product, irrespective of how much effective material may have been lost or discarded in the manufacturing process.

JOURNAL OF NEUROPHYSIOLOGY

A NEW medical journal, reflecting the rapid advance in our knowledge of the physiology of the nervous system, named the *Journal of Neurophysiology*, was issued for the first time in January, 1938. This journal has distinct aims, somewhat different from those of almost any other publication. In the first place, it plans to provide a channel for the prompt publication of original work, embracing all aspects of the subject amenable to experimental analysis. The journal will be published six times a year and an editorial board of three has been organized to reach prompt decisions on all contributions submitted. Papers to be published will be selected four weeks prior to their appearance, and it is hoped by this means that papers will actually appear in their printed form within two months or less after their receipt by the editors. This, along with a careful editorial policy in regard to literary form, should make this journal unique among medical publications. The members of the editorial board — J. G. Dusser de Barenne, J. F. Fulton and R. W. Gerard — are sufficiently well known in the field of neurology and physiology to justify the expectation that this journal will not only have a wide field of usefulness, but that the editors will uphold the strict rules which they have laid down. The *New England Journal of Medicine* extends its best wishes to this new journal of so much promise.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

M. FLETCHER EADES, M.D., *Secretary*
19 Bay State Road
Boston

CASE HISTORY No. 66. MARGINAL PLACENTA PREVIA

Mrs. M. B., aged thirty years, was seen at home on January 23, 1936, in the thirty-first week of her fourth pregnancy. Shortly before the visit she had passed some blood by vagina, "just like the beginning of a period." There was no pain or cramps.

Her family history was negative. Her past history included measles, mumps, chickenpox and pertussis in childhood and influenza at thirteen. Her tonsils had been removed at the age of four, and she had injured her right kidney in a coasting accident at sixteen without, however, any serious sequelae. Her catamenia, which began at twelve or thirteen, were of the twenty-six to twenty-eight-day type and lasted five or six days without pain. Her last period was June 25, making the expected date of labor April 1 to April 4. Mrs. B. had given birth to one child, who was now ten years of age. Her second and third pregnancies had been interrupted by induced abortions in 1928. The present pregnancy had been normal to date, and she had had no previous medical supervision.

Physical examination showed a well-developed and nourished woman, lying comfortably in bed and in excellent general condition. Her temperature was 98°F., pulse 80, respirations 20, and her blood pressure was 122 systolic, 74 diastolic. Her color was good, her eyes, nose, throat and neck were negative, and her teeth were well cared for. The breasts showed the usual signs of pregnancy. The heart showed no enlargement; there were no murmurs. The lungs were normal; there were no rales. The uterus corresponded in size to a seven months' pregnancy and was neither tender, spastic nor in labor. The fetus was presenting in LOA position, with the vertex unengaged; the fetal heart rate was 156. A vulvar pad worn by the patient showed a small amount of dark blood, and the total estimated quantity of blood lost did not exceed half an ounce.

The patient was at once transported by ambulance to the hospital, where further studies showed a urine negative for albumin and sugar, a hemoglobin of 70 per cent (Sahli), a red-blood-cell count 3,820,000 and a normal blood smear. X-rays taken for measurement of the fetal head by stereoroentgenometry showed the occipitofrontal diameter to be 10.3 cm.

A policy of watchful waiting was pursued because, first, the bleeding had been slight in amount and insufficient to jeopardize in itself the life of the patient or her baby; secondly, the latter was a dubious risk for immediate delivery by any method; and thirdly, the patient agreed to remain in the hospital until viability of the infant could be assured provided no further bleeding occurred. A very small amount of brown staining occurred on January 24 and January 30, while her general condition, blood pressure and urine remained normal. The slight degree of hypochromic anemia

A series of selected case histories by members of the section will be published weekly.
Comments and questions by subscribers are solicited and will be discussed by members of the section.

noted on admission was treated with ferrous sulfate, 12 gr. daily.

On February 12 x-ray examination showed the occipitofrontal diameter of the baby to be 11.3 cm., predicting an infant of minimum weight of 5 lb. On February 14 under gas-oxygen anesthesia and with all aseptic precautions, a vaginal examination was done which revealed the os to be easily patulous to one finger; the placental margin was felt 4 cm. within the internal os on the anterior surface of the lower uterine segment. An immediate abdominal cesarean section of the classical type was done with delivery of a 6 lb., 4 oz., female child in good condition. Both patient and baby made an uncomplicated recovery and left the hospital on March 3 in good condition, the baby weighing 6 lb., 6 oz.

Comment. Vaginal bleeding, no matter how slight in amount, in the early part of the last trimester of pregnancy must always be looked upon as potentially serious, as was done in this case. At this time, of course, the baby's viability is extremely doubtful no matter what method of delivery is contemplated. Hospitalization is imperative. Slight bleeding may be the precursor of extreme bleeding. A vaginal examination when the bleeding ceases to determine the exact cause of the bleeding is unwise because of the possibility of starting up a hemorrhage which will make delivery imperative to save the mother's life, and there is then practically no chance of a live baby. The use of x-ray measurements to determine the degree of prematurity is well worth while. In this case it gave results which definitely influenced the time of operation. It must be borne in mind, however, that it is not an infallible procedure as its results are not uniformly accurate. It may well have been, in spite of the successful outcome of this case, that another week or ten days before a final examination was undertaken would have assured a baby whose chance of survival would have been more enhanced by the extra period of intrauterine life, but it may be argued that if operation had been delayed ten days, a serious hemorrhage might have occurred. When any such case is examined, everything must be ready. There is no mention in this case of having a compatible donor at hand. This constitutes added safety for the mother and is a routine procedure which often saves life.

In the treatment of marginal placenta previa a bag is sometimes used, and sometimes the membranes are ruptured. Rupture of the membranes is rarely successful unless the patient is in labor. The use of a bag through an undilated cervix in a patient who is not in labor and is not bleeding is not so safe for the baby as an abdominal section. It carries with it the risk to the mother of added bleeding which the abdominal operation does not entail.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning April 11:

BARNSTABLE

The session scheduled for Easter Sunday, April 17, has been postponed to Sunday, May 1. John I. B. Vail, *Chairman.*

BERKSHIRE

Thursday, April 14, at 4:30 p. m., at the House of Mercy Hospital, Pittsfield. Subject: Early Syphilis. Instructor: Francis M. Thurmon. Melvin H. Walker, Jr., *Chairman.*

BRISTOL SOUTH (Fall River Section)

Monday, April 11, at 4:30 p. m., at the Union Hospital, Fall River. Subject: Cesarean Section, Analgesia. Instructor: M. Fletcher Eades. Howard P. Sawyer and Robert H. Goodwin, *Chairmen.*

ESSEX NORTH

Friday, April 15, at 4:30 p. m., at the Lawrence General Hospital, Lawrence. Subject: Cesarean Section, Analgesia. Instructor: M. Fletcher Eades. John Parr, *Chairman.*

FRANKLIN

Wednesday, April 13, at 8:00 p. m., at the Franklin County Hospital, Greenfield. Subject: Pneumococcus Pneumonia and Serum Therapy. Instructor: Frederick T. Lord. Halbert G. Stetson, *Chairman.*

HAMPDEN

Thursday, April 14, at 4:00 p. m., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and at 8:00 p. m., in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke. Subject: Some Complications of Labor: Analgesics in Labor. Instructor: Raymond S. Titus. George D. Henderson and George L. Schadt, *Chairmen.*

HAMPSHIRE

Wednesday, April 13, at 4:15 p. m., in the Nurses' Home, Cooley Dickinson Hospital, Northampton. Subject: Recent Advances in the Diagnosis and Treatment of Heart Disease. Instructor: Burton E. Hamilton. Warren P. Cordes, *Chairman.*

MIDDLESEX SOUTH

Wednesday, April 13, at 4:00 p. m., at the Cambridge Municipal Hospital, Cambridge Street, Cambridge. Subject: The Use of Vitamins in Pediatric Practice. Instructor: Louis K. Diamond. Edmund H. Robbins, *Chairman.*

NORFOLK

Friday, April 15, at 8:30 p. m., at the Norwood Hospital, Norwood. Subject: Acute Anterior Poliomyelitis — Its Diagnosis and Treatment. Instructor: Charles F. McKhann, Jr. Hugo B. C. Riemer, *Chairman.*

DEATH

TURNER—RALPH GORDON TURNER, M.D., of 1565 Main Street, Walpole, died at his home, March 26. He was in his thirty-second year.

Born in Marlboro, he was graduated from Dartmouth College in 1928 and received his degree from Rush Medical College, University of Chicago, in 1933.

Dr. Turner was a member of the American Medical Association, a fellow of the Massachusetts Medical Society and held memberships in the Phi Sigma Kappa and Alpha Kappa Kappa fraternities.

His widow, two brothers and his parents survive him.

MISCELLANY

COMMITTEE OF PHYSICIANS

Following the numerous discussions of the Principles and Proposals by medical societies throughout New England many physicians will doubtless be interested in an abbreviated form of the statement sent by the Committee of Physicians to the endorsers on March 2.

* * *

As a result of the editorial of October 16 in the *Journal of the American Medical Association* the Principles and Proposals with the list of signators were treated on November 7 to unfortunate publicity in the lay press, despite the best efforts of the committee. Especially unhappy was the general impression that the proponents of the Principles and Proposals were revolting against the American Medical Association. Although this impression arose directly from the *Journal of the American Medical Association* editorial, which had been released to the press before publication, the onus for the publicity fell largely on the committee. The immediate consequence was the withdrawal of a certain number of signatures and a sudden retardation in the growth of the list of endorsers. In addition to those who withdrew unconditionally a large number asked that their names be not used until they received further information concerning the past course and future intentions of the committee. (It is appropriate to state that very few of those who withdrew claimed that they were unaware of the nature or purpose of the Principles and Proposals.)

The *Journal of the American Medical Association* editorial had so misinterpreted the actions and intentions of the committee and the signators that it became at once apparent that the true issues raised by the Principles and Proposals were being obscured by discussion of irrelevancies. . . . At this time the most important immediate objectives in the opinion of the committee were to obtain a hearing before the Board of Trustees of the American Medical Association and to secure the right to state its position in the *Journal of the American Medical Association,* thus correcting the false impressions created by the editorial of October 16. Although a second editorial published on November 27 purported to have the sanction of the trustees, the committee had received no formal intimation that this body had taken any action with respect to the Principles and Proposals or their sponsors. They therefore on November 20 requested a hearing before this body and on December 8 asked the trustees to authorize publication in the *Journal of the American Medical Association* of a statement explaining the attitude and intent of the committee. At its meeting in December, the Board of Trustees of the American Medical Association invited the committee to send representatives to the meeting of the trustees in Chicago, February 17. Consideration of the publication of the committee's statement was postponed until the same date and all efforts of the committee to secure earlier action were fruitless.

On February 17 at 11 a. m. a delegation from the committee, consisting of Dr. Hugh Cabot, chairman, Drs. Cooley, Holt, Morgan, Osgood, Peters and Veeder, appeared before the Board of Trustees and presented the following statement:

> We appear before the Board of Trustees as delegates of a self-appointed committee, who represent the feelings of a considerable group of members of the American Medical Association. Interest in this common cause has in no sense altered the allegiance of this group to the American Medical Association. We therefore welcome the opportunity to appear before its governing body. The subject which we wish to discuss with you, first, is the purpose of the Principles and Proposals, which, we believe, have been both misunderstood and misinterpreted. Although these arose under the stimulus of the American Foundation's report, *American Medicine,* they were not derived from this report, nor did they emanate from the American Foundation or from any source other than the minds of certain members of this committee. After deliberation a consensus was achieved. It represents the greatest common denominator of these personal opinions concerning the directions which the policies of the organized medical profession of the United States should take in order to advance the quality of medical care. Its purpose was also to forestall untimely and unwise lay and governmental interference by demonstrating the openmindedness and declaring the good will of the medical profession and its desire to assert its prerogative as an expert body to lead all movements to improve medical care. It was hoped that the draft might create healthy discussion, and progressive action throughout the country if it were presented to the American Medical Association and its component societies. This feeling was strengthened by the reports of the reference committee to the House of Delegates at Atlantic City in 1937 concerning a slightly modified draft presented by the New York State delegation.
>
> Unfortunately, an editorial appeared in the *Journal of the American Medical Association* of October 16, condemning the Principles and Proposals and intimating that their authors and endorsers were acting in contravention of the policies of the American Medical Association and of the best interests of American medicine. This editorial and others which followed have, we believe, put an unfortunate color upon the publicity which the Principles and Proposals have received; they have beclouded the true issues with irrelevancies and have militated against the unprejudiced consideration of a subject which is as dear to the American Medical Association as to ourselves, namely the advancement of measures for the improvement of medical care.
>
> We therefore submitted for publication in the *Journal* of our association a statement of our attitude and intent, to correct what we consider to be erroneous impressions that have arisen from these editorials. This statement was presented to this board on December 8, 1937, two months ago. We believe that the democratic organization of the American Medical Association and the editorial integrity of the *Journal* justify us in asking this board to expedite its publication, which has already been long delayed. Behind

this request is a larger issue than the mere righting of a single wrong. It is the feeling in our minds that the *Journal* should maintain the same unprejudiced attitude toward the social and economic problems of medicine and public health that it holds toward clinical problems, providing an open forum with room for minority opinion and welcoming any new ideas which are honestly and intelligently presented. Furthermore, in our opinion the *Journal* should seek to stimulate similar free and open discussion among local medical societies and in local medical journals. We believe that if such an attitude is encouraged by the Board of Trustees, these Principles and Proposals will receive unprejudiced consideration before and at the 1938 meeting of the American Medical Association in California.

We are sure that your board will agree that if any argument or controversy arises it should be conducted in a dignified manner, on the usual plane of scientific disagreement by presentation of observation and inference, without recourse to irrelevant personalities and unsupported by the weapons of ridicule and innuendo which, we protest, have characterized certain editorials of our *Journal*.

We ask:

1. Publication in the *Journal* of our communication of December 8.
2. An agreement to open the pages of the *Journal* to reasonable and honest discussion of social and economic problems concerning the provision of medical care.
3. That all discussion of these problems be kept on a plane consonant with the dignity of the profession of medicine.
4. That you give us a prompt answer so that we may determine our future course.

After discussion that lasted until 3 p. m. the Board of Trustees passed the following votes:

1. That the statement submitted by the committee under date of December 8 for publication in the *Journal* be suitably edited, as are all communications offered for publication in that periodical, and that it be then submitted to the Committee of Physicians for approval.
2. That there be more discussion in the *Journal* of social and economic problems concerning the provision of medical care with the presentation of various aspects of the subject.

By agreement no notice of the purposes or results of the meeting were given to the press, except the statement that an amicable solution of the differences between the two parties might be expected.

On February 26 the committee convened in New York City to consider the results of the Chicago meeting. Before this there had been received from Dr. Morris Fishbein an edited version of the committee's statement together with an editorial comment. These were taken the same evening, with the criticisms of the committee, by Drs. Weiss and Peters to Dr. Fishbein, who was staying in New York. With one exception the suggestions of the committee were accepted. Both the editorial comment and the statement of attitude and intent were thereupon forwarded to the *Journal* for publication March 12 with the understanding that no additional remarks would be printed at this time. . . .

This objective having been attained it has become necessary to consider the further course of action of the committee and the signators.

The animosities first aroused by the public appearance of the Principles and Proposals are giving way to more mature consideration. There can be no doubt that the Principles and Proposals have aroused healthy discussion of the subject with which they are concerned.

Although the Principles and Proposals have no absolute value and should not be considered unalterable, they constitute the instrument which has united and stimulated a large group of physicians. The very general form of their statements allows latitude of interpretation without degradation of spirit and makes them a large common denominator of liberal medical opinion. For the present, then, they may well be retained entire as a tentative platform.

It is clearly recognized that the self-appointed committee should eventually give way to some more representative body appointed by democratic methods. Already, in the interests of more equitable representation, the committee has been enlarged. It now consists of the following men:

Dr. Russell L. Cecil (chairman), Dr. Hugh Cabot (vice-chairman), Dr. Milton C. Winternitz (vice-chairman), Dr. John P. Peters (secretary), Dr. George Blumer, Dr. Allan M. Butler, Dr. Louis Casamajor, Dr. Thomas B. Cooley, Dr. J. Rosslyn Earp, Dr. Channing Frothingham, Dr. L. Emmett Holt, Dr. William S. Ladd, Dr. William S. McCann, Dr. George R. Minot, Dr. Hugh Morgan, Dr. Robert B. Osgood, Dr. Richard M. Smith, Dr. John H. Stokes, Dr. Borden S. Veeder, Dr. James J. Waring, Dr. Soma Weiss.

The committee is receptive to suggestions for reorganization along representative democratic lines. . . . Suggestions from individual signators or groups of signators for a future program will also be welcomed. . . .

The committee has felt from the outset that the Principles and Proposals were composed by and for physicians. Although they have received the approval of great numbers of laymen and of lay organizations devoted to medical, social and economic projects, the committee has merely acknowledged this approbation. It has sedulously refused all offers of support from lay sources. It has even refrained from participation in public programs fostered or sponsored by lay groups. All its activities since November 7 have been financed by voluntary contributions from members of the committee and a small number of signators. . . .

INTERNATIONAL BROADCAST ON RHEUMATIC HEART DISEASE

Leading British and American physicians, 6000 miles apart, will confer via the radio on the greatest menace to child health, rheumatic heart disease. This conference, the first international broadcast on any health problem, will be heard over the Red Network of the National Broadcasting Company on Monday evening, May 2, at seven-thirty o'clock Eastern D.S.T. Arranged by the American Heart Association, the conference-broadcast will observe National Child Health Day.

Lord Thomas Jeeves Horder, physician-in-ordinary to the King of England, will open the conference speaking from London. Dr. Homer F. Swift, of the Rockefeller Institute, New York City, and Dr. T. Duckett Jones, of the House of the Good Samaritan, Boston, will then speak from Atlantic City where they will be attending the

annual meeting of the American Society for Clinical Investigation. Dr. William J. Kerr, president of the American Heart Association, will take up the discussion from San Francisco.

Rheumatic heart disease is now recognized as the deadliest and most crippling affliction of children of school age. Its annual mortality rate is seven times that of dread infantile paralysis during an epidemic, while every year it invisibly cripples thousands more. Close to a million persons in the United States have hearts damaged by rheumatic fever.

Lord Horder's discussion will dwell upon public-health aspects of the disease, particularly in England. The radio audience will then be carried to Atlantic City to hear Dr. Swift describe the medical investigations being carried on to isolate the cause of the disease. Dr. Jones will follow with a discussion of the treatment of children with crippled hearts, emphasizing the need for long-continued sanatorial care. Dr. Kerr, from the West Coast, will tell of the work of the American Heart Association in this field.

This international conference-broadcast was conceived by a committee of Irvington House, sanatorium for the care of children with heart disease at Irvington-on-Hudson, New York, in an effort to stimulate greater public interest and action in this major child-health problem. It will acquaint doctors, and particularly parents and teachers, with the challenge of rheumatic heart disease, more dangerous because of the lack of knowledge of its nature and the difficulty in recognizing its early symptoms. Although no effective cure has yet been found, it is hoped that this broadcast will be a first step in the earlier recognition of the disease which, if unchecked, finally incapacitates the heart. A widespread realization of its prevalence should encourage increased support of scientific studies along these lines.

The present difficulty in arousing the attention of the public to rheumatic heart disease lies partly in its undramatic nature. Compared with the explosiveness and rapid pace of most childhood diseases, it plays the triumphant but unspectacular role of the tortoise in the fable of the tortoise and the hare. It is not easy, without specific education, to recognize the first slow manifestations of rheumatic heart disease as the onset of a systemic disease which may forever cripple the heart of a child.

CONNECTICUT NEWS

New Head of New Haven Hospital

The Board of Directors of the New Haven Hospital has announced the appointment of James A. Hamilton, of Cleveland, Ohio, as superintendent of the hospital to succeed Dr. Albert W. Buck, who assumed the superintendency of the Charlotte Hungerford Hospital in Torrington on January 1.

Mr. Hamilton was graduated from Dartmouth College in 1922 and obtained his master's degree in 1923 from the Amos Tuck School of Business Administration. He was assistant professor of industrial management at Dartmouth from 1923 to 1936 and for ten years superintendent of the Mary Hitchcock Memorial Hospital at Hanover, New Hampshire. He is at the present time superintendent of the Cleveland City Hospital and lecturer at Western Reserve University. Mr. Hamilton plans to take up his work on September 1 after a summer vacation in California.

Dr. MacCarty of Mayo Foundation Speaks

Dr. William Carpenter MacCarty, professor of pathology at the Mayo Foundation at Rochester, Minnesota, and one of the nation's foremost authorities on cancer, was one of the speakers at the first of the 1938 meetings of the Association of Connecticut Tumor Clinics held at St. Francis Hospital on February 24. About 100 persons, among them representatives from hospitals throughout the State, attended the meeting over which Dr. L. P. Hastings, chairman of the tumor group, presided. Papers and clinical cases were presented by the members of St. Francis's staff, including Drs. Edward J. Whalen, Richard C. Buckley and Andrew F. Resnisky. Following the medical education meeting, those attending were entertained at a dinner as guests of the hospital.

Dr. Carl Wagner Opens Sanatorium

Dr. Carl P. Wagner, former senior psychiatrist at the Hartford Neuro-Psychiatric Institute of the Hartford Retreat, has opened a new private sanatorium for the treatment of a limited number of convalescent, nervous and mild mental patients on the former Alfred Gildersleeve estate on Marlborough Street, Portland.

The institution, called Elmcrest Manor, is on the crest of a hill overlooking the Connecticut Valley. It is housed in a large white mansion, built in 1815, set almost in the center of eight acres of grounds and surrounded by tall, old elm trees and formal gardens. There are separate three-bed wards for men and women patients, semi-private rooms and private rooms.

Dr. Wagner, a native of Culbertson, Nebraska, is a graduate of the University of Nebraska and of its College of Medicine. He has served as an instructor in psychiatry at the University of Colorado School of Medicine and from 1930 to 1932 was instructor in psychiatry at Yale University School of Medicine. For the last six years he has been senior psychiatrist at the Neuro-Psychiatric Institute.

Dr. Osborn, State Commissioner of Health, Injured

Dr. Stanley H. Osborn was injured on March 12 when his car left the road and turned over near the town of Ashford in Eastford. Dr. Osborn was removed to the Day-Kimball Hospital in Putnam.

Dr. Hunt Presents His Plan

Dr. Ernest L. Hunt, of Worcester, Massachusetts, presented his plan of voluntary co-operation of local medical and social-service organizations before a meeting in Hartford on March 9 sponsored by the Medical Information Bureau. This plan has been approved by the Council of the Massachusetts Medical Society but as yet has not been put into operation.

Hospital Insurance

Hospital insurance in Connecticut is already operating in New Haven, Waterbury, Milford and Norwalk. The plan sponsored by the State Hospital Association and now operating in the above-mentioned towns and cities except Norwalk probably will soon be extended throughout the State.

Robert Parnall, manager of the plan, says that the organization has just closed the twelfth enrollment month, and that a little more than 18,000 persons have joined the plan during its first year in New Haven. The figure is about 10 per cent of the population of the city. About a month ago the hospitals in Waterbury were accepted as "member hospitals," and residents of Waterbury were elected to the Board of Directors of the plan, which is

incorporated as a nonprofit organization. The Aetna Life Insurance Company is offering a plan for hospitalization insurance, very similar to that established by the Plan for Hospital Care. Under both, insurance is limited to groups employed in stores, factories, offices and industries. Groups of 10 persons employed by the same firm, and their families, are insurable under the Plan for Hospital Care. The Aetna plan has been launched among concerns that now carry group life-insurance policies with the company, and requires signatures of 75 per cent of the employees covered by the group life policy. Only actual employees are covered, but it is said that the service will soon be extended to include the members of their families.

The Aetna plan provides benefits of $4.00 a day at monthly cost to the insured of 77 cents. Coverage is for seventy days during any one disability, except that if the disability is due to pregnancy the benefits are for a maximum of fourteen days. In addition to the benefit, the employee, under the Aetna plan, is entitled to reimbursement for any fees actually charged for anesthetics or their administration, for the use of operating room and for laboratory fees, excluding x-ray fees, up to a maximum, during any one disability, of five times the daily benefit. Employees under seventy years of age are eligible and may be insured until that age is reached.

The Plan for Hospital Care limits the benefits to twenty-one days in any one year, and covers a bed in semi-private accommodations, meals, general nursing care, operating-room service, all medications, all surgical dressings, routine laboratory services, oxygen and serums, basal metabolism tests, ambulance service within three miles radius of the member hospital, maternity delivery-room service (one year after subscriber joins plan) and ordinary nursery care of newborn baby. If any subscriber takes a private room, he is allowed $4.50 a day credit on its cost. If he is taken to a non-member hospital, he receives a cash credit of $6.00 a day against his bill. For 50 cents a month additional, the wife or husband of a subscriber is covered, and for 25 cents a month all children that have not reached their nineteenth birthday are included. Dependents of subscribers, however, are required to pay the hospitals $1.00 a day to get the same benefits that are payable to subscribers. The Plan for Hospital Care does not accept persons who have reached their sixty-sixth birthday, but once one is enrolled one may continue indefinitely. The Plan for Hospital Care does not include the cost of anesthesia, physiotherapy, x-ray and electrocardiography.

Neither plan makes any provision for the payment of physicians' and surgeons' fees. Neither plan permits an individual to join independently of the groups in which he is employed, and in both plans the premiums are paid by the employers, who are authorized by the insured to deduct them from their pay each month.

Doctors Alone Eligible for Health Posts

Every town, city and borough in Connecticut must have a health officer who is a licensed practitioner of medicine according to an opinion handed down by the Deputy Attorney. The law does not require, however, that the health officer be a resident of the town or city where he officiates.

Results of Premarital Blood Test

From data available for 1937 there were considerably more cases of syphilis uncovered as a result of the premarital blood test than in 1936. Syphilis occurred about equally in men and women. From the standpoint of prevention of congenital syphilis the tests on women are most important.

Inspection of Indoor Water Pollution

The first local survey of water supplies of buildings was started in Hartford in 1937. Since then surveys have been started in New Haven, Bridgeport, New Britain and Waterbury. In the Hartford inspection from March through December, ninety-six buildings were included. Inadequately protected drinking-water tanks were found, and several direct connections to sewers from water lines through refrigeration and air-conditioning equipment were discovered. In all cases building owners and managers have been willing and even anxious to make any desired improvements after the hazards have been explained.

Health-Officer Appointments

Ernest R. Pendleton, M.D., has been appointed health officer of Granby replacing Mr. Wesley N. Clark, resigned.

Eugene N. Cozzolino, M.D., has been appointed health officer of West Haven to fill the vacancy caused by the death of Charles E. Kaufman, M.D.

H. R. Hansell, M.D., has been appointed health officer of Sharon during the absence of Jerome S. Chaffee, M.D.

John E. Stoddard, M.D., has been appointed health officer of Meriden to succeed Michael J. Sullivan, M.D.

Winfield E. Wight, M.D., has been appointed health officer of Thomaston to replace J. H. Kane, M.D., resigned.

Deaths

O'CONNELL — Thomas S. O'Connell, M.D., seventy-one, of 59 Burnside Avenue, East Hartford, for nearly half a century a practicing physician in that town and its representative in the last session of the General Assembly, died at St. Francis Hospital, February 25, after a long illness.

For forty years a member of the East Hartford School Board, Dr. O'Connell had long been an outstanding member of the High School Committee besides serving as school physician. He was also an East Hartford fire-district commissioner, and served several terms as Democratic town chairman. He was examining physician for several insurance companies and for many lodges.

Born in Colchester, December 15, 1866, he was educated in the public schools and at Bacon Academy. He began to teach school when he was nineteen years old, and four years later entered the Baltimore College of Physicians and Surgeons. He was graduated near the top of his class in 1892. His practice in East Hartford opened in August, 1892, was continued until his final illness.

He leaves a son, Judge Richard D. O'Connell, of the East Hartford Town Court; a daughter, Mrs. Frederick Welsh, of Irvington, New Jersey; two brothers, Judge Michael D. O'Connell, of Stafford Springs, and John O'Connell, of Lynn, Massachusetts; two sisters, Miss Margaret O'Connell, who lived with him in East Hartford and Miss Anne O'Connell, of Colchester; and two grandchildren.

PRATT — Edward Loomis Pratt, M.D., seventy-nine, a leading physician in Winsted for fifty-three years and one of the founders of the Litchfield County Hospital, died March 4.

Dr. Pratt was born November 2, 1858, in Ravenna, Ohio, the son of Dr. Henry Pratt and Anna (Barnes)

Pratt. He graduated from New York University in 1884 and went to Winsted in February, 1885, to begin the practice of medicine. Named a director of Litchfield County Hospital when it was founded, he had served in that capacity since that time and was a member of both the medical and surgical staffs. He was visiting physician at the William L. Gilbert Home for forty-five years. He was a member of the county and national medical societies, Litchfield County University Club and the Second Congregational Church, and a trustee of the Gilbert School and Gilbert Home. He leaves his widow, Elizabeth (Alvord) Pratt; a son, Henry G. Pratt; a sister, Miss Ella Pratt; and two grandchildren, Charlotte and Margaret Pratt, all of Winsted.

TUBERCULOSIS BOOKLETS

Two booklets on tuberculosis, one for patients and the other for the "doctor of the future," will be made available this spring by the National Tuberculosis Association and its affiliated groups throughout the country to senior students in Grade A medical schools. Dr. Kendall Emerson, managing director of the National Tuberculosis Association, has announced that this is part of the service of the tuberculosis groups to carry on their educational activities among the physicians, as well as among the general public.

In Massachusetts the schools receiving this service are: Harvard Medical School, Tufts College Medical School and Boston University School of Medicine.

"To the credit of the American doctor," the booklet for students says, "the record shows that he has from the beginning of the organized fight against tuberculosis generously joined hands with the nonmedical crusader, fully agreeing with him that tuberculosis is not merely a disease of certain tissues but a social problem of first magnitude. This fine record should forever silence the criticism that doctors' interests are too narrowly limited to sick organs."

In its message to the students, the National Tuberculosis Association says, "The hope of eradicating tuberculosis lies in the hands of the doctors of tomorrow."

What You Should Know About Tuberculosis is the title of the booklet written for the patient. It is an interpretative booklet, offered as an aid to the physician in guiding his patient. Its tone is optimistic, and the language is simple.

ANNIVERSARY MEETING OF THE MEDICAL SERVICE, PETER BENT BRIGHAM HOSPITAL

An anniversary meeting in celebration of twenty-five years' work of the Medical Service of the Peter Bent Brigham Hospital was held in the amphitheater of the hospital on March 31.

At the opening of this department in 1913, Dr. Henry A. Christian was physician-in-chief, as he is now. The others on the staff at that time were as follows: Channing Frothingham, Jr., physician; Francis W. Peabody, resident physician; I. Chandler Walker, assistant resident physician; Reginald Fitz, house officer in charge of O. D. D.; Roger P. Dawson, senior house officer; Wilson G. Smillie, junior house officer; Warren R. Sisson, subjunior house officer; and Frances Burnham-Myles, head nurse, Ward F.

The program included a presentation of three of the first four cases admitted to the service and a talk by Dr. Christian on "Certain Concepts of Bright's Disease Based on Twenty-Five Years' Experience at the Peter Bent Brigham Hospital."

CORRESPONDENCE

LIVER PREPARATIONS CONFORMING TO U.S.P. STANDARDS

To the Editor: When liver and stomach preparations were admitted to the *U.S. Pharmacopoeia,* Eleventh Edition, it was recognized that these products presented a different problem, from the viewpoint of standardization, than any question previously before the Committee of Revision.

As no ordinary methods for standardization or testing were available, an advisory board, made up of specialists in the treatment of anemia, was appointed. This board established methods for determining the value of anti-anemia products, and the basis for a U.S.P. "unit of potency." It also issued forms for reporting evidence of clinical value and announced regulations for indicating the potency of U.S.P. products and for the wording of the labels.

On the invitation of the board, a large number of clinical reports were submitted by manufacturers in evidence of the value of their products, and the board, after reviewing these records, herewith submits its conclusions. This first report lists the products which have been approved up to this time as complying with the U.S.P. specifications and the firms authorized to sell or distribute them.

As is probably generally known, only a relatively small group of manufacturers have provided the necessary hospital facilities for checking the clinical value of anti-anemia products as required by the board, and several of these distribute their products through the medium of other pharmaceutical firms.

Having been supplied with adequate clinical evidence of the efficiency of a manufacturer's product and having accepted it as U.S.P. grade with a specific dose, the board, on request, has also authorized the distribution of some of these approved products by other firms when the firms have given assurance that their handling of the products will in no way alter their quality or potency. No doubt the board will later report additional approved preparations and firms.

E. Fullerton Cook, *Chairman,*
Committee of Revision.

43rd Street and Woodland Avenue,
Philadelphia, Pennsylvania.

* * *

REPORT ON LIVER PRODUCTS BY THE *UNITED STATES PHARMACOPOEIA* ANTI-ANEMIA PREPARATIONS ADVISORY BOARD

The standardization of products for the treatment of pernicious anemia is defined for the first time by the Eleventh Revision of the *U.S. Pharmacopoeia* as follows: "Liver, stomach and other preparations used for this purpose, to be recognized as meeting the specifications of this *Pharmacopoeia,* must be approved by the U.S.P. Anti-anemia Preparations Advisory Board. Approved products must have complied with the following specifications: (1) there shall have been submitted from time to time, as requested by the board, satisfactory clinical data from treatment, with the product in question, of cases of Addisonian pernicious anemia; (2) the clinical data submitted shall satisfy the U.S.P. Anti-anemia Preparations Advisory Board that the administration of the material in question, as prepared from liver or stomach, can produce a satisfactory result in the dose given."

In accordance with this requirement, the U.S.P. Anti-anemia Preparations Advisory Board has considered data submitted by various pharmaceutical companies. In each

case the response of the patient to the liver extract in question was studied particularly with respect to the reticulocyte and red-blood-cell production resulting from the daily administration of a uniform amount of each preparation. The nature of the preparations submitted has been either dry liver extract (extractum hepatis), liquid extract of liver (liquor hepatis) or parenteral solution of liver (liquor hepatis purificatus), as defined in the *U.S. Pharmacopoeia,* Eleventh Revision.

Because of the variation in the efficiency of different processes of manufacture, the therapeutic activity of the final product does not necessarily correspond to the amount of liver from which it was derived. It is therefore necessary to define the therapeutic activity of the final product in other terms. Accordingly, the board has assigned to each acceptable preparation a value in terms of units. The amount of material constituting a "unit" is considered to be that amount of material which, when given daily to patients with pernicious anemia, has produced a satisfactory hematopoietic response. Since in the average case material derived from about thirty times as much liver must be given by mouth to produce the same response as when given by injection, it has been necessary to define the "unit" either as an "oral" unit or as an "injectable" unit, according to the intended method of administration of each preparation.

Accordingly, it is understood that on labels, bottles or cartons, or in advertising circulars, the manufacturer whose products have been assigned unitage by the board shall no longer state the number of grams of liver employed in making the preparation, but merely either the number of cubic centimeters or grams of material constituting a unit. Depending on the method to be used in the administration of the preparation, the unit will be defined as either an "oral" unit or an "injectable" unit. Definition of the number of units in a preparation for "oral" administration in terms of "injectable" units or vice versa is not permitted. It is further understood that if any dosage is suggested by the manufacturer, the dosage recommended should not be less than one unit a day, whether given daily or at longer intervals. The wording on the label or in the package literature concerning the unitage will give the following information: "The daily (oral, intramuscular) administration of——(no. gm., cc.) (capsules, teaspoons, and so forth) of material prepared by the method employed in producing the contents of this (bottle, vial, package, and so forth) has been demonstrated to produce a satisfactory hematopoeitic response in pernicious anemia, and constitutes a unit according to the *U.S. Pharmacopoeia* Anti-anemia Preparations Advisory Board."

In general it is recommended that, without good evidence that no harm will result, the amount of material administered should probably not be less than one unit a day, whether given daily or in multiple amounts at longer intervals. In many instances it is probable that the clinical indications will render it advisable to give the patient much more than a dosage averaging a unit a day. It must be recognized that the amount of material constituting a unit is determined largely on the basis of the hematopoietic response and does not imply that such an amount is necessarily effective in the control of gastrointestinal or neural manifestations. Furthermore, there is some evidence that the effectiveness of different types of preparations, although similar when defined in terms of units with respect to blood formation, may differ in their effectiveness upon the gastrointestinal or neural manifestations. A full discussion of the indications for the administration of liver preparations is obviously outside the scope of this announcement; through the co-operation of the American Medical Association and the Committee of Revision of the *U.S. Pharmacopoeia,* a special article on this subject has been published, "The Use of Drugs in the Treatment of Anemia" (J. A. M. A. *107;* 1633-1636, 1936).

The board will, as occasion arises, re-evaluate products based on new clinical data or assign unitage to new products submitted by manufacturers and accepted by the board.

U.S. Pharmacopoeia Anti-Anemia Preparations Advisory Board,
C. W. Edmunds, M.D., *Chairman,*
William B. Castle, M.D.,
Raphael Isaacs, M.D.,
George R. Minot, M.D.,
W. W. Palmer, M.D.

* * *

The Anti-anemia Preparations Advisory Board has designated below the unitage of the acceptable liver products of the following manufacturers and distributors:

Abbott Laboratories, North Chicago, Illinois

1. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
   In the following dilutions:
   (a) 0.1 cc. equals 1 unit (injectable).
   (b) 0.2 cc. equals 1 unit (injectable).
2. Extractum Hepatis. Dry Liver Extract.
   Powder in capsules. 50 capsules (25 gm.) equal 1 unit (oral).

Armour and Company, Chicago, Illinois

1. Liquor Hepatis. Liquid Extract of Liver.
   45 cc. equal 1 unit (oral).
2. Extractum Hepatis. Dry Liver Extract.
   9 capsules (4.5 gm.) equal 1 unit (oral).

Basic Endocrines, Inc., San Francisco, California

Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).

George A. Breon and Company Inc., Kansas City, Missouri

Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).
(c) 0.3 cc. equals 1 unit (injectable).
(d) 0.4 cc. equals 1 unit (injectable).

Buffalo Pharmacal Co., Buffalo, New York

1. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
   0.2 cc. equals 1 unit (injectable).
2. Extractum Hepatis. Dry Liver Extract.
   50 capsules (25 gm.) equal 1 unit (oral).

Carroll Dunham Smith Pharmacal Co., Orange, New Jersey

Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).

Chappel Laboratories, Rockford, Illinois

1. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
   2.5 cc. equal 1 unit (injectable).
2. Liquor Hepatis. Liquid Extract of Liver.
   60 cc. equal 1 unit (oral).

Chemical Works of Gedeon Richter, Inc., Budapest, Hungary
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
2 cc. equal 1 unit (injectable).

Cheplin Biological Laboratories, Syracuse, New York
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.4 cc. equals 1 unit (injectable).

The Columbus Pharmacal Co., Columbus, Ohio
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).

Direct Sales Company, Inc., Buffalo, New York
Extractum Hepatis. Dry Liver Extract.
(a) 5 vials (25 gm.) equal 1 unit (oral).
(b) 50 capsules (25 gm.) equal 1 unit (oral).

The Drug Products Co., Inc., Long Island City, New York
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.1 cc. equals 1 unit (injectable).

Ethko Chemical Products Co., New York, New York
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.4 cc. equals 1 unit (injectable).

Flint Eaton and Company, Decatur, Illinois
1. Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).

C. E. Jamieson and Company, Detroit, Michigan
Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm). equal 1 unit (oral).

Jensen-Salsbery Laboratories, Inc., Kansas City, Missouri
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.4 cc. equals 1 unit (injectable).

Kremers-Urban Company, Milwaukee, Wisconsin
Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).

The Lakeside Laboratories, Milwaukee, Wisconsin
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).

Lederle Laboratories, Pearl River, New York
1. Liquor Hepatis. Liquid Extract of Liver.
60 cc. equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
(a) 0.06 cc. equals 1 unit (injectable).
(b) 0.3 cc. equals 1 unit (injectable).

Eli Lilly and Company, Indianapolis, Indiana
Extractum Hepatis. Dry Liver Extract.
3 vials (12.75 gm.) equal 1 unit (oral).

The Maltbie Chemical Co., Newark, New Jersey
Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).

The S. E. Massengill Co., Bristol, Tennessee
1. Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).
(c) 0.4 cc. equals 1 unit (injectable).

McNeil Laboratories, Inc., Philadelphia, Pennsylvania
1. Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.2 cc. equals 1 unit (injectable).

The William S. Merrell Company, Cincinnati, Ohio
Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).

Metropolitan Laboratories, New York, New York
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.4 cc. equals 1 unit (injectable).

Montgomery Ward and Co., Chicago, Illinois
Extractum Hepatis. Dry Liver Extract.
75 capsules (25 gm.) equal 1 unit (oral).

The National Drug Company, Philadelphia, Pennsylvania
1. Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).
(c) 1.0 cc. equals 1 unit (injectable).

Parke, Davis and Company, Detroit, Michigan
1. Extractum Hepatis. Dry Liver Extract.
6 vials (24 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
2.0 cc. equal 1 unit (injectable).

Pitman-Moore Company, Indianapolis, Indiana
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).

Premo Pharmaceutical Laboratories, Inc., New York, New York
Extractum Hepatis. Dry Liver Extract.
(a) 50 capsules (25 gm.) equal 1 unit (oral).
(b) 5 vials (25 gm.) equal 1 unit (oral).

Raymer Pharmacal Co., Philadelphia, Pennsylvania
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.1 cc. equals 1 unit (injectable).

William H. Rorer, Inc., Philadelphia, Pennsylvania
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.2 cc. equals 1 unit (injectable).

Leonard A. Seltzer Company, Detroit, Michigan
1. Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.1 cc. equals 1 unit (injectable).

Sharp and Dohme, Inc., Philadelphia, Pennsylvania
Extractum Hepatis. Dry Liver Extract.
(a) 50 capsules (25 gm.) equal 1 unit (oral).
(b) 5 vials (25 gm.) equal 1 unit (oral).

G. H. Sherman, M.D., Inc., Detroit, Michigan
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.2 cc. equals 1 unit (injectable).

The Smith-Dorsey Company, Lincoln, Nebraska
1. Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).

United Drug Co., Boston, Massachusetts
Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).

U. S. Standard Products Company, Woodworth, Wisconsin
1. Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).

The Upjohn Company, Kalamazoo, Michigan
1. Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).

Valentine Meat Juice Company, Richmond, Virginia
1. Liquor Hepatis. Liquid Extract of Liver.
45 cc. equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 1.0 cc. equals 1 unit (injectable).
(b) 1.5 cc. equal 1 unit (injectable).

The Warren-Teed Products Company, Columbus, Ohio
Extractum Hepatis. Dry Liver Extract.
50 capsules (25 gm.) equal 1 unit (oral).

Western Research Laboratories, Denyer, Colorado
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.4 cc. equals 1 unit (injectable).

The Wilson Laboratories, Chicago, Illinois
1. Extractum Hepatis. Dry Liver Extract.
(a) 50 capsules (25 gm.) equal 1 unit (oral).
(b) 5 vials (25 gm.) equal 1 unit (oral).
2. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.1 cc. equals 1 unit (injectable).
(b) 0.2 cc. equals 1 unit (injectable).
(c) 0.3 cc. equals 1 unit (injectable).
(d) 0.4 cc. equals 1 unit (injectable).

Winthrop Chemical Company, New York, New York
Liquor Hepatis Purificatus. Parenteral Solution of Liver.
0.1 cc. equals 1 unit (injectable).

The Zemmer Company, Pittsburgh, Pennsylvania
1. Liquor Hepatis. Liquid Extract of Liver.
45 cc. equal 1 unit (oral).
2. Extractum Hepatis. Dry Liver Extract.
75 capsules (25 gm.) equal 1 unit (oral).
3. Liquor Hepatis Purificatus. Parenteral Solution of Liver.
In the following dilutions:
(a) 0.4 cc. equals 1 unit (injectable).
(b) 0.1 cc. equals 1 unit (injectable).

The board will, as occasion arises, issue supplementary announcements either as a revaluation of the above products based upon new clinical data or to make a report upon new products which are submitted.

NOTICES

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Thursday, April 21, in the Peter Bent Brigham Hospital amphitheater (Shattuck Street entrance), at 8:15 p. m.

PROGRAM

Adrenalin Sensitivity in Hyperthyroidism. Dr. Emil Goetsch, professor of surgery, Long Island College of Medicine.

The Value of Antitoxin in Scarlet Fever. Dr. Francis G. Blake, Sterling Professor of Medicine, Yale University School of Medicine.

Medical students and physicians are cordially invited to attend.

MARSHALL N. FULTON, M.D., *Secretary.*

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on *Wednesday, April 20,* at 12 o'clock noon. *Note change of day and date.*

Dr. Allan M. Butler and Dr. David L. Lionberger will discuss "Principles and Proposals."

All physicians are cordially invited to attend.

JOHN B. HALL, M.D., *Secretary.*

COURSE IN OCCUPATIONAL DERMATOSES

During May, 1938, a course in occupational dermatoses will be given under the auspices of the Harvard School of Public Health. Lectures will be given on the clinical manifestations, aspects, and so forth. Clinics will be held at the Massachusetts General Hospital, and at the offices of various insurance companies. Visits to some of the more important factories will be arranged, so that students may study industrial processes and preventive measures. The number of students will be limited to ten. Further information and registration blanks may be obtained from the Dean of the Harvard School of Public Health, 25 Shattuck Street, Boston, Mass.

TUMOR CLINIC, BOSTON DISPENSARY

Each Tuesday and Friday morning from ten to twelve-thirty there is a meeting of the Tumor Clinic of the Boston Dispensary, a unit of the New England Medical Center. All kinds of tumors are seen, discussed, and when indicated, treated with radium and high-voltage x-ray.

Physicians are welcome to visit this clinic and bring patients to the clinic for diagnosis.

BOSTON CITY HOSPITAL

The monthly conference of clinical pathology will be held at the Boston City Hospital on Wednesday, April 13, at 12 o'clock noon, in the pathological amphitheater.

JOSEPH E. HALLISEY, M.D., *Secretary*,
Medical Staff.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, APRIL 11

TUESDAY, APRIL 12

*9-10 a. m. Boston Dispensary. Vitamin A Deficiency in Adults. Dr. Harold J. Jeghers.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

WEDNESDAY, APRIL 13

*9-10 a. m. Boston Dispensary. Hospital case presentation. Dr. S. J. Thannhauser.

*12 m. Clinicopathological conference. Children's Hospital amphitheater.

12 m. Boston City Hospital, pathological amphitheater. Monthly conference of clinical pathology.

THURSDAY, APRIL 14

8:30-9:30 a. m. Exchange visit, surgical and orthopedic staffs of the Peter Bent Brigham and Children's hospitals, held this week at the Children's Hospital.

*9-10 a. m. Boston Dispensary. Transurethral Prostatic Resection. Dr. P. N. Papas and Dr. Harold A. Chamberlin.

FRIDAY, APRIL 15

*9-10 a. m. Boston Dispensary. Acid-Base Balance in Health and Disease. Dr. John H. Talbott.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

12 m. Clinical meeting of the children's medical service, Massachusetts General Hospital, Ether Dome.

SATURDAY, APRIL 16

*9-10 a. m. Boston Dispensary. Hospital case presentation. Dr. Thannhauser.

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.

APRIL 13 — Boston City Hospital, pathological amphitheater. Conference on clinical pathology. Notice above.

APRIL 13 — New England Dermatological Society. Page 584, issue of March 31.

APRIL 13 — New Bedford Cancer Clinic. Page 546, issue of March 24.

APRIL 13 — Eastern Hampden Medical Association. Page 499, issue of March 17.

APRIL 14 — Pentucket Association of Physicians. Hotel Bartlett, 95 Main Street, Haverhill, 8:30 p. m.

APRIL 18 — Boston Medical History Club. Boston Medical Library, 8 Fenway, Boston.

APRIL 18, 19 and 20 — Thomas William Salmon Memorial Lectures. Page 450, issue of March 10.

APRIL 20 — South End Medical Club. Page 623.

APRIL 21 — Harvard Medical Society. Page 623.

APRIL 22 — Symposium in Honor of Dr. Jelliffe. Page 583, issue of March 31.

APRIL 23 — Massachusetts Memorial Hospitals, annual reunion of house officers' alumni association. Page 546, issue of March 24.

APRIL 26 — New England Society of Psychiatry. Page 322, issue of February 17.

MAY 16 and 17 — American Neisserian Medical Society. Page 582, issue of March 31.

MAY 31, JUNE 1 and 2 — Annual meeting of the Massachusetts Medical Society. Hotel Bradford, Boston.

JUNE 6, 7, 8, and 9 — American Association of Industrial Physicians. Page 499, issue of March 17.

JUNE 13-17 — American Medical Association. San Francisco.

JUNE 13, OCTOBER 8 and NOVEMBER 15 — American Board of Ophthalmology. Page 282, issue of February 10.

SEPTEMBER 12-14 — American Association for the Study of Goiter. Page 545, issue of March 24.

OCTOBER 17-21 — Clinical Congress of the American College of Surgeons, New York City.

OCTOBER 24-26 — Academy of Physical Medicine, scientific session. Washington, D. C.

DISTRICT MEDICAL SOCIETIES

BRISTOL SOUTH

MAY 5 — 5 p. m., New Bedford.

ESSEX SOUTH

MAY 5 — Censors meet at Salem Hospital, 3:30 p. m.

MAY 11 — Annual meeting, Salem Country Club, Peabody. Dinner at 7 p. m. Speaker and subject to be announced.

FRANKLIN

Meeting will be held at the Franklin County Hospital, Greenfield, at 11 a. m. the second Tuesday of May.

HAMPDEN

Meetings will be held on the fourth Tuesday in April and July.

HAMPSHIRE

MAY 11 — Page 546, issue of March 24.

MIDDLESEX EAST

Meeting will be held at the Bear Hill Golf Club, Stoneham, at 12:15 p. m. on May 11.

MIDDLESEX NORTH

Meeting will be held at the Vesper Country Club, Lowell, on April 27.

NORFOLK DISTRICT

MAY — Annual meeting.

The censors meet on the first Thursdays of May and November in each year.

NORFOLK SOUTH

Meetings held at 12 noon.

MAY 5 — Annual meeting, at 12 noon.

PLYMOUTH

Meetings will be held at 11 a. m. on April 21, May 19 and July 21.

WORCESTER

APRIL 13 — Hahnemann Hospital, Worcester. Dinner will be at 6:15, to be followed by business session and scientific program.

MAY 11 — Afternoon and evening, annual meeting. Place and schedule of program to be announced.

BOOKS RECEIVED FOR REVIEW

Operative Gynecology. Harry Sturgeon Crossen and Robert James Crossen. Fifth edition. 1076 pp. St. Louis: The C. V. Mosby Company, 1938. $12.50.

Theoretical Principles of Roentgen Therapy. Edited by Ernst A. Pohle. 271 pp. Philadelphia: Lea & Febiger, 1938. $4.50.

Milestones in Medicine: Laity lectures of the New York Academy of Medicine. 276 pp. New York and London: D. Appleton-Century Company, 1938. $2.00.

Clinical and Experimental Investigations in Agranulocytosis: With special reference to the etiology. Preben Plum. 410 pp. Copenhagen: Nyt Nordisk Forlag; London: H. K. Lewis & Co., Ltd., 1937. 18/-.

Essentials of Prescription Writing. Cary Eggleston. Sixth edition, revised. 155 pp. Philadelphia and London: W. B. Saunders Company, 1938. $1.50.

Surgical Diseases of the Mouth and Jaws. Earl Calvin Padgett. 807 pp. Philadelphia and London: W. B. Saunders Company, 1938. $10.00.

The Physician's Business: Practical and economic aspects of medicine. George D. Wolf. 384 pp. Philadelphia, London, New York and Montreal: J. B. Lippincott Company, 1938. $5.00.

Handbook on Nasal Accessory Sinuses. Frank L. Alloway. 121 pp. Kingsport, Tennessee: Kingsport Press, Inc., 1937. $2.00.

Malnutrition the Medical Octopus. John Preston Sutherland. 368 pp. Boston: Meador Publishing Company, 1937. $3.00.

Alcohol: One man's meat. Edward A. Strecker and Francis T. Chambers, Jr. 230 pp. New York: The Macmillan Company, 1938. $2.50.

Man Against Himself. Karl A. Menninger. 485 pp. New York: Harcourt, Brace and Company, 1938. $3.75.

Diseases of Women for the General Practitioner. Paul Titus. Edited by Morris Fishbein. 320 pp. New York: National Medical Book Co., Inc., 1937. $4.00.

The Conquest of Cholera: America's greatest scourge. J. S. Chambers. 366 pp. New York: The Macmillan Company, 1938. $4.75.

Digestive Tract Pain: Diagnosis and treatment; experimental observations. Chester M. Jones. 152 pp. New York: The Macmillan Company, 1938. $2.50.

Sir Kenelm Digby: Writer, bibliophile and protagonist of William Harvey. John F. Fulton. 75 pp. New York: Peter and Katharine Oliver, 1937. $5.00

BOOK REVIEWS

Short Years: The life and letters of John Bruce MacCallum, M.D., 1876-1906. Archibald Malloch. 343 pp. Chicago: Normandie House, 1938. $3.50.

Dr. Malloch has interspersed in this fascinating narrative of the life of one of the most promising young scientists that American medicine has produced, selections from his voluminous correspondence, and "memories" which appear in his notebooks. With this intimate picture of MacCallum's intellectual development is an account of his many valuable contributions based upon his studies in embryology, histology, physiology and pharmacology, many of which were made during his medical school career, and all within the period between 1892 and 1906. Paralleling this scientific activity in point of time and equaling it in literary interest is a small but select group of prose and poetic writings reflecting a philosophy of life uncommon to the pure scientist.

There seems to have been something imparted to the students in the Canadian schools that fostered qualities in them that we have been taught to expect and have come so much to admire—a breadth of view and an imaginative insight accentuating the keenly scientific temperament. We have only to recall Sir William Osler and "Jack" McCrae, not to mention Archibald Malloch, himself, the author of this memoir.

Osler's earlier years find their counterpart in MacCallum's early youth. Both were intensely interested in natural history and were meticulously accurate in observation and the recording of their facts. In his struggle with the disease, which from the very beginning of his career fastened itself upon him, one is reminded of Robert Louis Stevenson, and as with him, so with MacCallum, the reader is torn between admiration for the fortitude with which he bore his affliction and the variety and extent of his accomplishments. It is this that constitutes one of the principal charms of this delightful narrative.

Born in Dunnville, Ontario, in 1876, receiving his preliminary education at home and his collegiate training at the University of Toronto, he came under the influence of Mall, Osler, Welch and the remarkable group of teachers at Johns Hopkins in 1896. Owing to the condition of his health he was obliged to seek for occupation in a climate suited to his physical infirmities. For a time he was in practice in Denver and then took a position in the University of California with Professor Loeb; it was there that the rest of his life was passed and much of his scientific work was accomplished, subject to numerous interruptions because of exacerbations of his tuberculosis. It was there, also, that death overtook him, suddenly, in 1906, terminating a career of great promise just as he was entering upon his thirtieth year.

This book should be a stimulus to every medical man and for that matter to everyone for whom science and the humanities hold any appeal.

Mental Therapy: Studies in fifty cases. Louis S. London. Vol. 1 and 2. 1201 pp. New York: Covici, Friede, Publishers, 1937. $12.50.

These two volumes are an extensive treatise on psychoanalysis illustrated by fifty detailed case histories which are reported in a clear and interesting style and with a serious scientific approach. The reviewer agrees with the author's statement that psychiatry and psychoanalysis are interwoven; an analyst without a knowledge of psychiatry is compared with an internist who does not know pathology or a surgeon who is ignorant of anatomy.

At first the author had a Freudian analytic training, but later he worked with Stekel on dream analysis and investigated his active technic. Many of the analyses in this book are carried out by means of dream interpretation; the dreams are symbolically interpreted and the author, under Stekel's influence, makes dream symbolism the center not only of dream investigation but also of the technic of psychoanalysis. By this progressive dream analysis and an active intervention in the life of the patient, Stekel shortened the time required, as he believed that lengthy analyses were undesirable. The reviewer feels that this kind of analysis is merely a superimposed intellectual interpretation, as the complete working through of the neurotic conflicts requires a longer time. It is true that short analyses may relieve neurotic symptoms, but they do not eliminate the unconscious roots of the neurosis. However, in fairness to the author, it must be remembered that he states on page 277 of the first volume that dreams cannot be analyzed according to a stereotyped symbolism; the free associations of the patient must be connected to the manifest dream content before the cryptic meaning of the dream can be solved. Many of the author's analyses are of considerable length.

The book is divided into six parts and discusses, in turn, metapsychology, psychosexual psychology and pathology, the various neuroses, sexual perversions, and psychoses. The author believes that much can be done for schizophrenia if the analysis is begun in the early stages of the disease; but the analytic therapy is fraught with great difficulties due to the incomplete transference.

In the chapter "Psychosexual Pathology of the Sexual Instinct," the author develops a theory which involves "traumatization of the libido." This trauma liberates

the components of homosexuality, perversion and narcissism. It must be pointed out that this viewpoint is not new, as it is generally admitted that the libido is always traumatized in anxiety situations. Furthermore, he interprets narcissism as abnormal, whereas it is generally accepted that narcissism is not a perversion but exists in every living creature.

These volumes give the impression that more importance is attached to the analytic material and dream symbolism than to the usual procedure of the dynamic interpretation of the analytic situation; the latter is always indicated, but perhaps too briefly.

A Pediatrician in Search of Mental Hygiene. Bronson Crothers. 271 pp. New York: The Commonwealth Fund, 1937. $2.00.

This book, which for the purpose of clarity and completeness, has been conveniently divided into three sections, represents a thorough and careful study of the present confused positions of the pediatrician, psychiatrist, psychologist and social worker in the field of mental hygiene, and offers a tentative plan whereby an intelligent and practical solution may be evolved for the benefit of the patient and to the satisfaction of those concerned. As the author states he is not interested "in perfecting a blend of the various virtues of each, nor in supervising a 'job analysis,' but in discovering ways of co-operation between them, which will enrich the knowledge of the pediatrician and contribute to the health of the child." Since the field of pediatrics has progressively broadened, it is natural that mental hygiene should at least be recognized by the pediatrician, but at the same time the pediatrician should realize that neither previous training nor time qualifies him to be the director of such an organized unit. His position should be that of adviser to the group and to the parents. If such an arrangement could be reached, both the psychiatrist and the pediatrician would be in a better position to understand the scope and interrelation of their respective work. Dr. Crothers stresses the importance of the pediatrician's principal duty, which is the treatment of organic diseases as they occur in children and not the practice of psychiatry. The importance and necessity of an intern's thorough knowledge of these organic disturbances is also discussed, but at the same time he points out how a competently directed clinic conducted in a children's hospital can give both the student and the intern adequate training to appreciate the mental as well as the physical aspect of the child. The entire volume is written in the frank and straightforward manner so characteristic of the author, and should prove of value to all who read it.

The Physician's Business: Practical and economic aspects of medicine. George D. Wolf. 384 pp. Philadelphia, London, New York and Montreal: J. B. Lippincott Company, 1938. $5.00.

This book is an interesting compilation of the ethical principles governing medical practice, together with associated problems which may be studied with profit by all groups of physicians, and especially by those students who are about to graduate from medical schools, because it depicts the responsibilities and opportunities facing the hospital intern and his subsequent years of practice.

Adequate space is devoted to medical economics and the practitioner's financial problems with appropriate advice as to ways and means by which to secure material success.

Although some space is given to a discussion of comparatively simple household problems, which have little to do with the practice of medicine, the observations and advice given furnish interesting reading which will be appreciated by many.

The book closes with a chapter devoted to the "Trends in Medical Practice," with the associated controversies before the public and the profession, but without a solution of the questions under discussion.

This volume contains a great deal of useful information and sound advice which warrants careful reading.

Sir Kenelm Digby: Writer, bibliophile and protagonist of William Harvey. John F. Fulton. 75 pp. New York: Peter and Katharine Oliver, 1937. $5.00.

An exhibit of works by and about Sir Kenelm Digby, largely from the collection of the author, was shown at the Grolier Club in New York City in April and May, 1937. As an introduction to the demonstration of this superb collection, Professor Fulton has written an explanation, including a brief life of Digby, an estimation of his character, and an interpretation of the value of his work to medicine. Digby's life was an exceedingly dramatic one and he lived in a time which was marked by extreme activity. Digby is known as a collector of books, a pirate in the Mediterranean, a famous lover, and a protagonist of William Harvey. Although Digby's physiology was mainly Galenical, he accepted Harvey and attempted to harmonize the new ideas about the circulation of the blood with a well-systematized scheme of bodily function. Digby was also in close touch with Descartes during his years in Paris and it seems probable that Digby's ideas in regard to reflex action came directly from Descartes. Digby must, therefore, be considered as one of the early supporters of the modern conception of the nervous system.

Professor Fulton feels that Digby's scientific life has been neglected. There has been much written about his position in philosophy, his powerful influence as a patron of letters and his extraordinary gift as a letter writer, but few have noticed his relations with William Harvey or with Descartes.

This book, from a private press, is beautifully gotten up, with superb illustrations and a most pleasing type of print as well as cover. In contents, as well as in appearance, it is a choice item and the individual must be considered fortunate who owns one of the three hundred copies which have been printed.

A Textbook of Ophthalmology. Sanford R. Gifford. 492 pp. Philadelphia and London: W. B. Saunders Company, 1938. $4.00.

This textbook was written for the use of the medical student or the general practitioner making his first contact with the field of ophthalmology. For the beginner, it is desirable that a text be interesting, lucid in expression and informative in illustration. Gifford's text meets these requirements, and it shows evidence of wisdom in deciding what to omit as well as what to include for the beginner. Of the 492 pages of the text, 62 pages are used to outline methods of examination of the eye, and 30 pages to index the contents.

For the purpose for which it was written, Gifford's text may be regarded as a classic. Its effectiveness is enhanced by 249 well-executed illustrations, and by 10 color plates.